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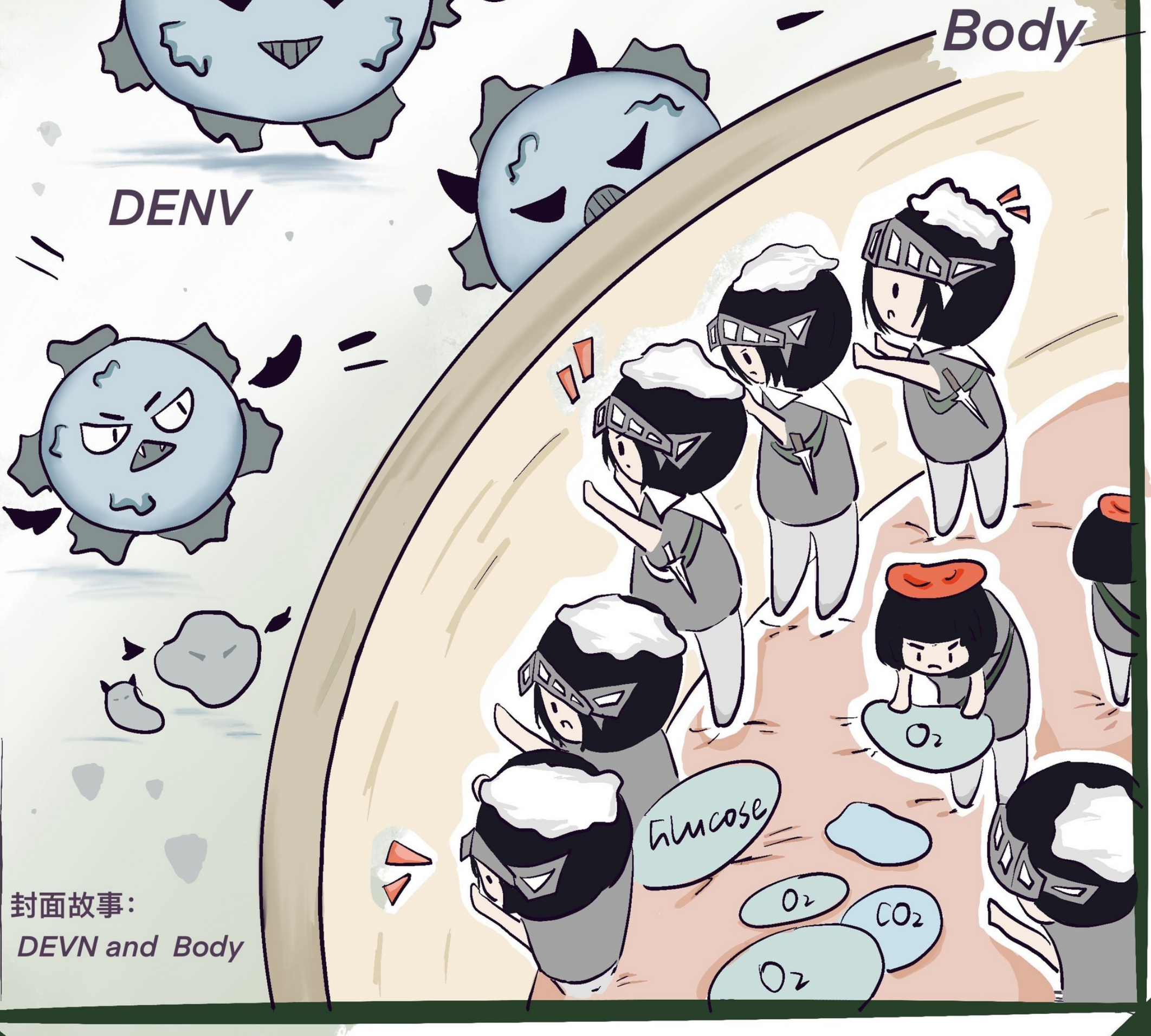


封面故事：

DEVN and Body

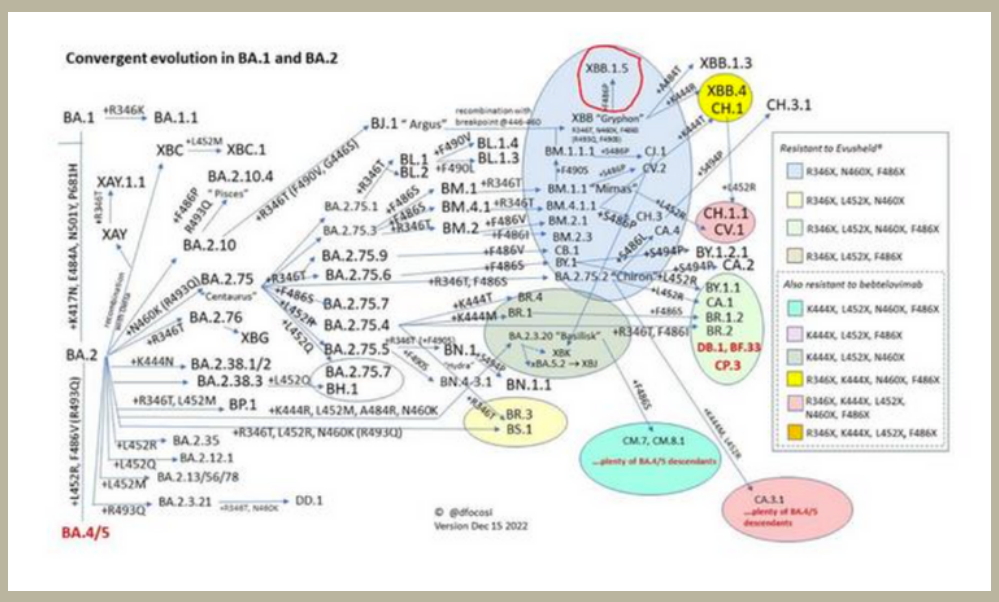
摘要

SARS-CoV-2 奥密克戎的 BQ 和 XBB 亚变异现在正在迅速扩大，这可能是由于其额外的尖峰突变导致的抗体逃避特性的改变。来自疫苗接种者和感染者的血清对 BQ.1、BQ.1.1， XBB 和 XBB.1 的中和能力明显受损，包括来自使用 WA1 / BA.5 二价 mRNA 疫苗增强的个体的 血清。针对 BQ 和 XBB 亚变异的滴度分别降低了 13 至 81 倍和 66 至 155 倍，远远超出了迄今 为止观察到的水平。能够中和原始奥密克戎变异株的单克隆抗体对这些新的亚变异株基本上 没有活性，并且确定了单个尖峰突变。发现这些亚变异具有与其前辈相似的 ACE2 结合亲和 力。总之，BQ 和 XBB 亚变异对当前的疫情形势构成严重威胁，使所有授权抗体失效，并且可 能因其在逃避抗体方面的优势而在人群中占据主导地位。

作者：Ray & Olivia

XBB 新变种可能带来的风险挑战与防护

关键词:
免疫逃逸; 传播速率; 重组毒株;
ACE2; RBD 结合域; 变异;



导致 XBB1.5 出现的关键性突变 F486P。

一、前言

严重急性呼吸综合征冠状病毒 2(SARS-CoV-2)新变种的不断出现引起了连续的全球感 染浪潮。在 SARS-CoV-2 系的命名惯例中，前缀 "X "表示通过两个或多个亚变体之间的基因 重组产生的血统。XBB 系是在 人类宿主与两个奥密克戎的亚变体，即 BA.2.10.1 和 BA.2.75 自然共感染后出现的。它在 2022 年夏季首次被印度的公共卫生部门发现。XBB.1.5 是原始XBB 亚变体的直系后裔。

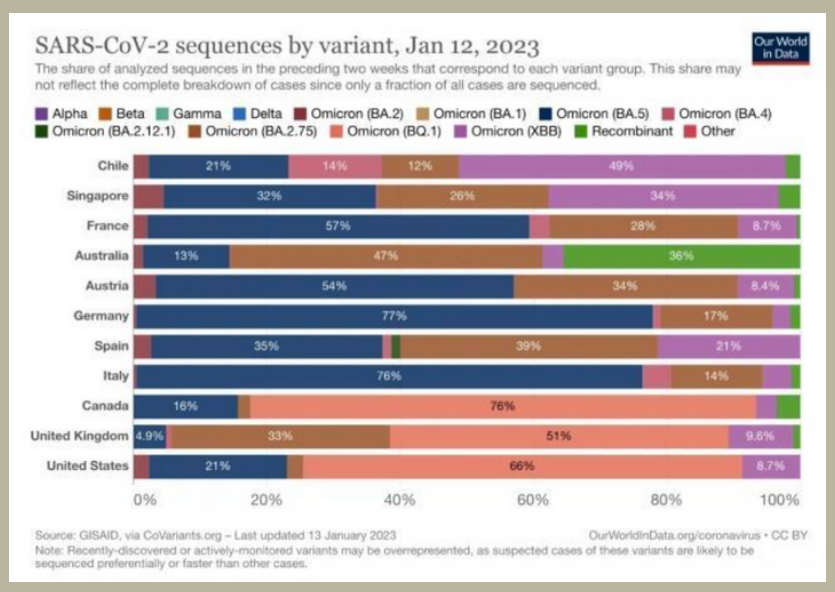
自 2021 年 11 月在南非发布第一份报告以来，奥密克戎因其高传播性和免疫逃避而成 为主导变种 1，2，随着时间的推移，许多奥密克戎亚谱系不断涌现。最初的奥密克戎 BA.1 被 BA.2 取代，BA.2 进一步演变为 BA.2.12.1，BA.2.75，BA.2.75.2，BA.4 和 BA.5，其中 BA.5 目前在许多国家占主导地位。BA.4 和 BA.5 具有相同的尖峰序列(以下定义为BA.4/5)，它们的后代 BA.4.6，BF.7 和 BQ.1.1 正在扩大患病率。截至 2022 年 11 月 19 日，BA.2 衍生的亚系 BA.2.75.2 占美国 SARS-CoV-2 感染总数的 0.8%，而 BA.4/5 衍生的亚谱系 BA.4.6、BF.7、BQ.1 和 BQ.1.1 分别占总病例的 4.4%、7.8%、25.5%和 24.2%。此外，另一 个 BA.5 衍生的亚谱系 XBB 于 2022 年 8 月在印度首次发现，正在欧洲迅速传播，并已在 美国被发现。XBB 在新加坡占主导地位，占 2022 年 10 月 3 日至 9 日这一周 SARS-CoV-2 感 染的 54%。所以 XBB.1.5 可以说是迄今为止基因最丰富和最具传播性的 SARS-CoV-2 亚变 体。

二、传播地域

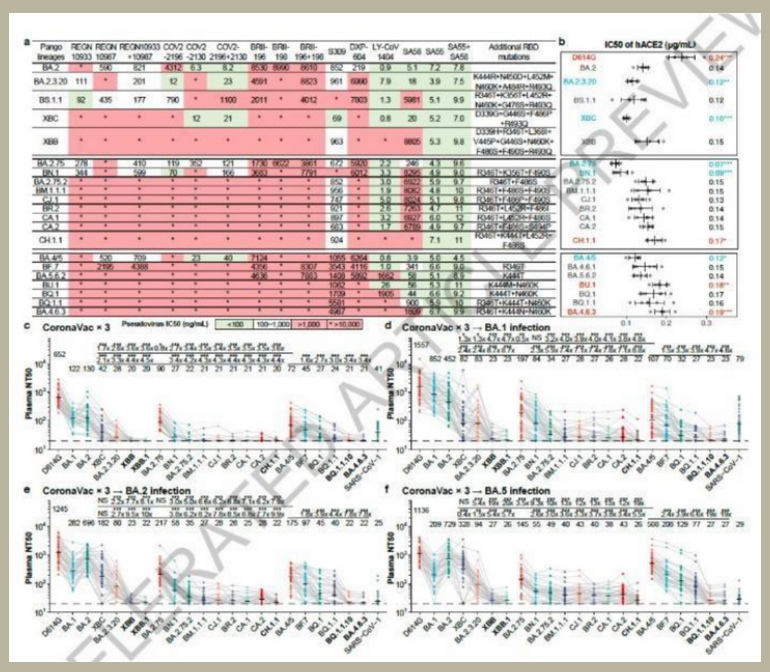
根据世界卫生组织的数据，XBB.1.5 至少在 38 个国家流行，在美国的流行率最高， 它占全国 COVID-19 病例的大约 43%。在美国国内，由 XBB.1.5 引起的病例比例有很大的 地理差异，从中西部的 7%到新英格兰地区的 70%以上。

澳大利亚、加拿大、欧盟、日本、科威特、俄罗斯、新加坡、南非和英国的政府机 构也已正式报告了 XBB.1.5。实时监测数据显示，XBB.1.5 正在全球范围内迅速蔓延， 并可能成为下一个主导的亚变体。

> “实时监测数据显示，XBB.1.5 正在全球范围内迅速蔓延， 并可能成为下一个主导的亚变体。”



在美国、欧洲和其他地方的城市污水处理系统中也检测到了 XBB.1.5。



三、风险与挑战

科学家们在《细胞》杂志上在线发表的一项研究中发现，BQ 和 XBB 亚变体 "几乎不受疫 苗的影响"，包括新的 Omicron 增强剂。他们写道:“这可能会导致突破性感染和再感染的 激增，尽管这些疫苗已经被证明能够抵御严重的疾病。”根据一项新的研究，最近几个月成 为主导的 omicron 亚变体对新增强剂的有效性构成了严重威胁，使抗体治疗无效，并可能导 致突破性感染的激增。

哥伦比亚大学和密歇根大学的科学家表示，BQ.1、BQ.1.1、XBB 和 XBB.1 omicron 亚变 体是迄今为止 Covid-19 中最具免疫逃避性的变体。根据美国疾病控制和预防中心的数据，这 些变体加在一起，目前在美国造成 72%的新感染。科学家们在周二在线发表在同行评议杂志 《细胞》上的一项研究中发现，这些亚变体 "几乎不受疫苗的影响"，包括新的欧米茄增强 剂。接种过疫苗的人在突破性地感染了之前的 omicron 变体后，对亚变体的免疫反应也比较 弱。

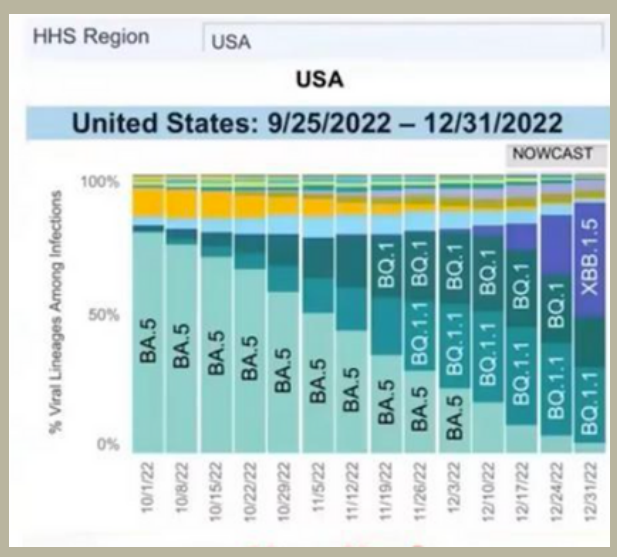
截止到 2022 年 12 月 31 日，通过美国政府公开的 数据显示，BA.5 几乎是瞬间被后起之秀 BQ.1、XBB.1.5 等毒株压制。不过只通过纵向的对比总是不够充分的， 我们将病毒的传播 30%时间做一个横向对比的话，我们 可以很明显的看到，XBB.1.5 仅仅使用了 17 天占比就已 经达到了 30%，同期的 BQ.1 毒株 26 天才能达到。对于 新出现的变种 XBB、XBB.1.5，其是一种奥密克戎亚型变 异毒株由 BJ.1 和 BM.1.1.1 重组而来。国际上，欧美国 家已经逐渐显示出，XBB 是优势毒株，主要表现为传播 力和免疫逃逸能力增加。但其致病力和奥密克戎其他系 列变异株没有明显区别，重症率和死亡率在流行 XBB 的 这些国家没有显著增加。研究指出，XBB 致病力并未明 显增强，但由于毒株突变能更好地与人体细胞受体结 合，XBB.1.5 传染性大幅增加。

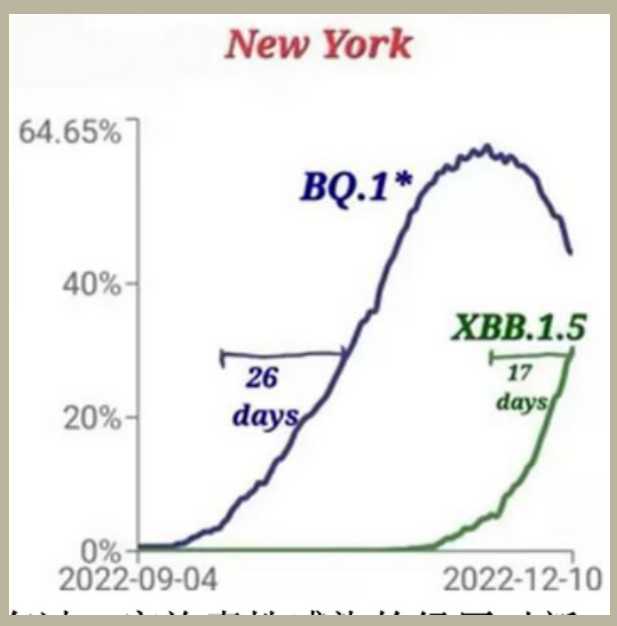
同时现在重组毒株 XBB.1.5 作为新冠病毒的“最新 版本”，我们印象中通过感染其他新冠病毒来产生抗体 的方法通过一定的研究证实事实上效果并不好。研究结 果显示对于接种了三针疫苗且感了 BA.2、BA.5 毒株的
人群来说 XBB.1 中和滴度并不高。也就是说打过疫苗并且有过 B 家族毒株感染的经历对新 的XBB系列

毒株并不会有太好的防护效果

免疫学上存在一个很有意思的现象——免疫记忆。记忆 B 细胞是其中的关键角色，它们
在人体第一次接触病毒时在淋巴结中产生。然后，这些细胞在血液中监视同样的敌人，准备 发展成浆细胞，然后大量产生抗体。当免疫系统遇到类似但不完全相同的病毒株时，问题就 来了。在这种情况下，记忆 B 细胞反应开始发挥作用，而不是产生新的 B 细胞来产生量身定 制的抗体。这通常会导致旧抗体的产生，这些抗体结合在新旧菌株中发现的特征，被称为交 叉反应抗体。它们可能提供一些保护，但并不是完全适合新菌株。

同时 cell 这篇论文通过不同地区的变异株占比生动显示了我们面临的复杂情况，同时 将 B 家族毒株与 XBB 家族重组毒株进行对比，发现很多单抗对 XBB、XBB.1 直接无效，其免 疫逃逸尤其明显，与此同时其刺突蛋白与 ACE2 受体的结合不弱于其他的新冠毒株。也就是 提醒我们说整个 XBB 家族的传播性并没有降低但是面对对于免疫系统的攻击是有其他毒株没 有的增益的。





四、防护方法

尽管美国爆发的数据还需要进行更多的科学研究来进行论证支撑，但 XBB.1.5 拥有强大 的免疫逃逸能力，这一点毋庸置疑。一旦 XBB.1.5 病毒在我国境内蔓延，将会引发国内的第 二次疫情爆发。在面对 XBB.1.5 的时候，我们需要做一些准备工作。

1.加强对疫情资料的统计

随着全国疫情管控方式的优化，国内对核酸检测的相关限制也基本解除，所以想要获得 准确的诊断结果并不容易。数据来源的不准确会增加病毒大规模传播的风险。如今大数据 技术高度发达，我们需要有足够的力量来提升疾病的数据质量。

2.加速开发新型药物

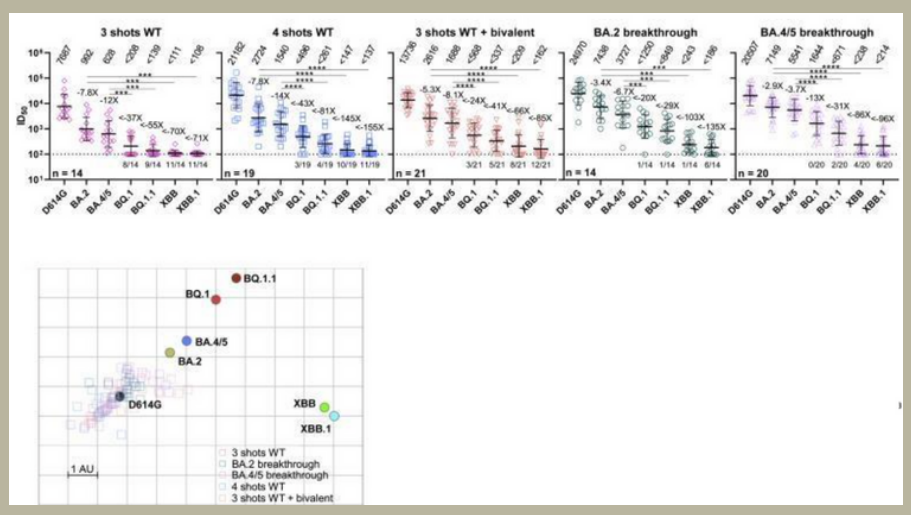
XBB.1.5 在美国创造了十万人 1.524 的平均死亡率纪录，原因在于辉瑞公司的新冠疫苗
并不像我们认为的那样有效。为避免类似美国那样的情况在国内发生，国内的科研单位要在 最短时间内研制出一种新型抗新冠病毒的药物，且其效果要优于辉瑞公司的特效药物。

3.个人依旧要做好防护 坚持勤洗手、戴口罩、常通风、公筷制，保持社交距离、咳嗽礼仪、清洁消毒等卫生习
惯，即使感染新冠病毒康复以后，也应做好个人防护;坚持良好的生活习惯，规律作息、避 免熬夜，合理膳食、适度饮酒，多吃新鲜蔬菜、水果，适量运动、保持良好心态;减少聚餐 聚会，缩短聚餐时间，可以通过视频、电话传递祝福，尤其是避免把感染风险带给家中的老 年人;加强健康监测，密切关注自身和家人的健康状况，如果出现发热、干咳、乏力、咽痛 等症状，或者核酸或抗原检测阳性，要尽可能待在通风好、相对独立的房间，尽量减少与同 住人员接触，密切关注病情进展，如果出现病情加重，要及时就医。

五、总结

到 2023 年，XBB、XBB.1.5 等新冠病毒的变种将是全球现阶段面临的最大敌人，也是最 难以对抗的敌人。在优化疫情防控措施的情况下，人类与病毒的共生是必然的，而我们也没有办法阻止这种病毒的发生，到 2023 年，XBB、XBB.1.5 等新冠病毒的变种将是全球现阶段面临的最大，也是最难以对抗的敌人。在优化疫情防控措施的情况下，人类与病毒的共 生依旧是必然的，因此，我们必须要做好准备。

我们也不要在面对新挑战时过于慌张 要做到兼听则明，偏听则暗。



“在优化疫情防控措施的情况下，人类与病毒的共生是必然的，而我们也没有办法阻止这种病毒的发生。。。”

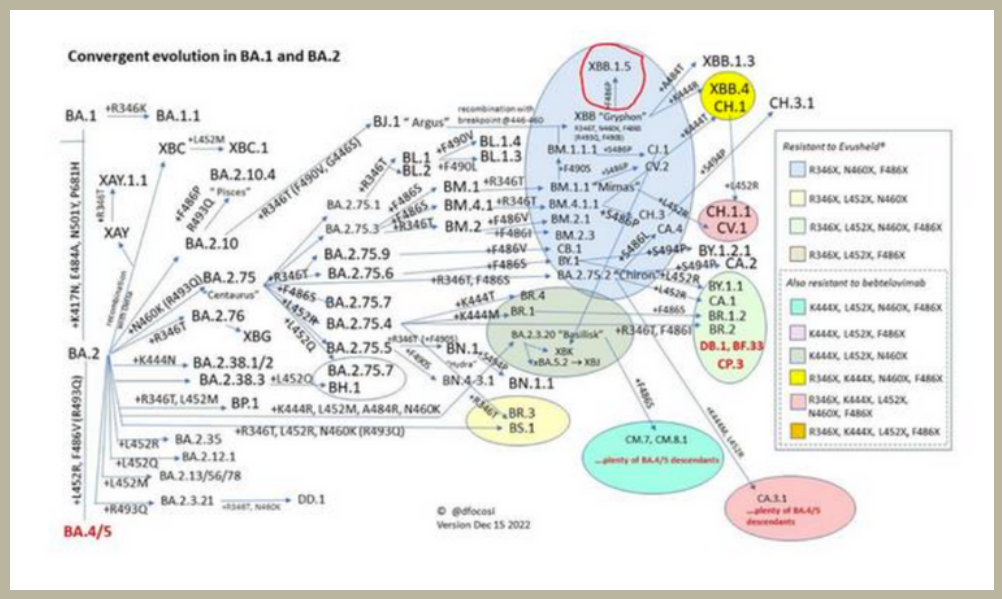
Abstract

The BQ and XBB subvariants of SARS-CoV-2 Omicron are now rapidly expanding, possibly due to their additional spike mutations resulting in altered antibody evasion properties. Sera from vaccinated and infected individuals have significantly impaired neutralization of BQ.1, BQ.1.1, XBB and XBB.1, including sera from individuals boosted with the WA1/BA.5 bivalent mRNA vaccine. The titers against the BQ and XBB subvariants were reduced by 13- to 81-fold and 66- to 155-fold, respectively, well beyond the levels observed to date. Monoclonal antibodies capable of neutralizing the original Omicron variant were largely inactive against these new subvariants, and a single spike mutation was identified. These subvariants were found to have similar ACE2 binding affinity to their predecessors. In conclusion, the BQ and XBB subvariants pose a serious threat to the current epidemic situation, rendering all licensed antibodies inactive and potentially dominant in the population due to their superiority in evading antibodies.

authors：Ray & Olivia

Possible Risk Challenges and Protection from New XBB Variants

Keywords: immune escape; transmission rate; recombinant strain; ACE2; RBD binding domain; mutation; bivalent vaccine; risk assessment

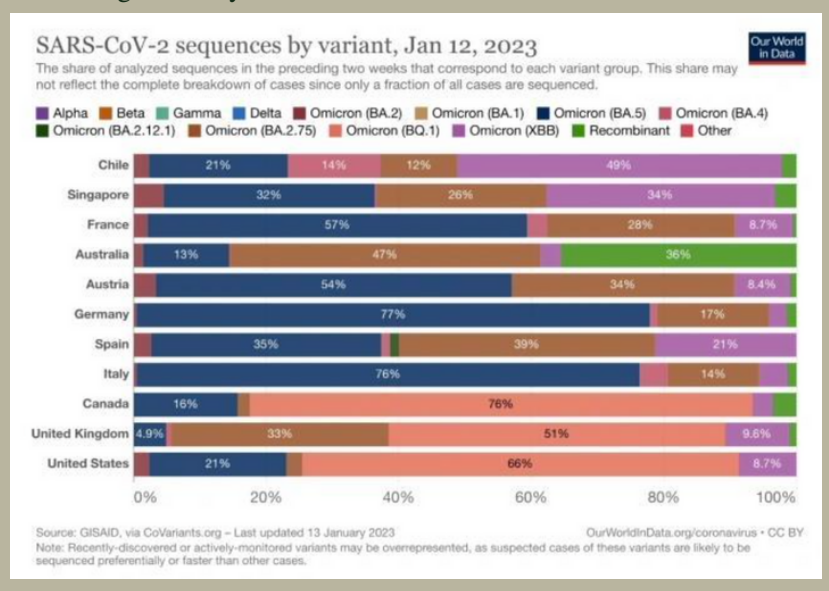


The key mutation responsible for XBB1.5, F486P

I. Preface

The emergence of new variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused successive waves of global infections. In the nomenclature convention for the SARS-CoV-2 lineage, the prefix "X" denotes a lineage generated through genetic recombination between two or more subvariants. the XBB lineage emerged after natural co-infection of human hosts with two subvariants of Omicron, BA.2.10.1 and BA.2.75. XBB.1.5 is a direct descendant of the original XBB subvariant.

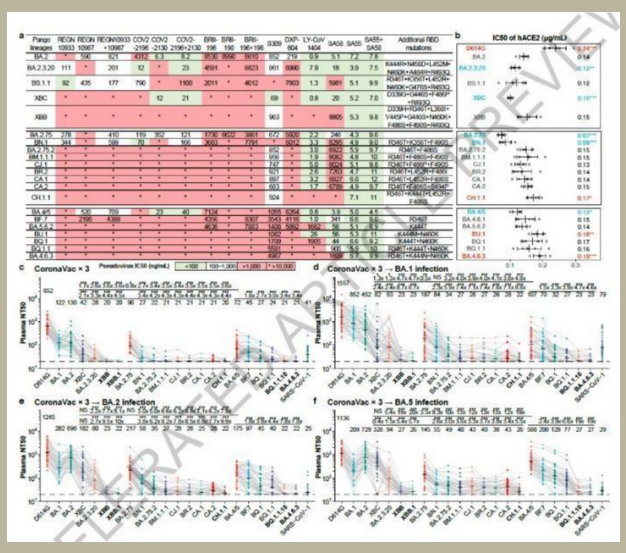
Since the first report in South Africa in November 2021, Omicron has become the dominant variant due to its high transmission and immune evasion.1,2 Over time, many Omicron subgenera have emerged. The original Omicron BA.1 was replaced by BA.2, which further evolved into BA.2.12.1, BA.2.75, BA.2.75.2, BA.4 and BA.5, of which BA.5 is now dominant in many countries. BA.4 and BA.5 share the same spike sequence (hereafter defined as BA.4/5), and their descendants BA.4.6, BF.7 and BQ.7 are the dominant variants. BF.7 and BQ.1.1 are expanding in prevalence. As of November 19, 2022, the BA.2-derived subline BA.2.75.2 accounts for 0.8% of all SARS-CoV-2 infections in the United States, while the BA.4/5-derived subseries BA.4.6, BF.7, BQ.1, and BQ.1.1 account for 4.4%, 7.8%, 25.5%, and 24.2% of total cases, respectively. In addition, another BA.5-derived subspectrum, XBB, was first identified in India in August 2022, is spreading rapidly in Europe, and has been identified in the U.S. XBB dominates in Singapore, accounting for 54% of SARS-CoV-2 infections for the week of October 3-9, 2022. Therefore, XBB.1.5 is arguably the most genetically abundant and transmissible SARS-CoV-2 subvariant to date.



II. Geographical spread

According to the World Health Organization, XBB.1.5 is endemic in at least 38 countries, with the highest prevalence in the United States, where it accounts for approximately 43% of COVID-19 cases nationwide. Within the United States, the proportion of cases caused by XBB.1.5 varies widely geographically, from 7% in the Midwest to more than 70% in New England.

XBB.1.5 has also been officially reported by government agencies in Australia, Canada, the European Union, Japan, Kuwait, Russia, Singapore, South Africa, and the U.K. Real-time surveillance data indicate that XBB.1.5 is spreading rapidly worldwide and may become the next dominant subvariant.



XBB.1.5 has also been detected in municipal wastewater treatment systems in the United States, Europe, and elsewhere.

III. Risk challenges

In a study published online in the journal Cell, the scientists found that the BQ and XBB subvariants were "virtually unaffected by the vaccine," including the new Omicron enhancer. This could lead to a surge in breakthrough infections and reinfections, even though these vaccines have been shown to protect against serious diseases, they write. According to a new study, the omicron subvariants that have become dominant in recent months pose a serious threat to the effectiveness of the new boosters, rendering antibody therapy ineffective and potentially leading to a spike in breakthrough infections.

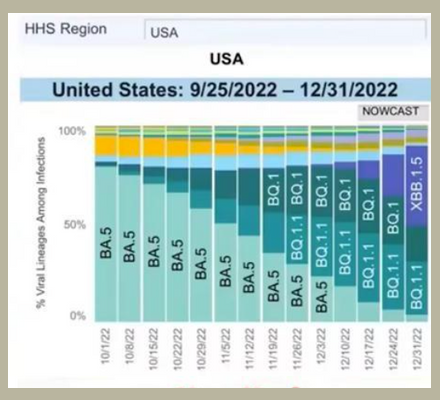
Scientists at Columbia University and the University of Michigan say that the BQ.1, BQ.1.1, XBB and XBB.1 omicron subvariants are by far the most immune evasive variants of Covid-19. Together, these variants currently cause 72 percent of new infections in the United States, according to the Centers for Disease Control and Prevention. In a study published online Tuesday in the peer-reviewed journal Cell, the scientists found that these subvariants are "virtually unaffected by the vaccine," including the new omega booster. Vaccinated individuals with breakthrough infections with the previous omicron variants also had weaker immune responses to the subvariants.

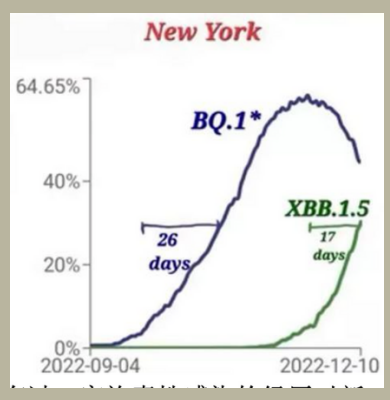
As of December 31, 2022, BA.5 was almost instantly overpowered by the up-and-coming BQ.1 and XBB.1.5 strains, as shown by data made public by the US government. However, a vertical comparison is not sufficient, so if we compare the spread of the virus in 30% of the time, we can clearly see that XBB.1.5 has already reached 30% after only 17 days, while the BQ.1 strain took 26 days to reach it. The new variant XBB, XBB.1.5, is a variant of the Omicron subtype recombined from BJ.1 and BM.1.1.1. Internationally, European and American countries have gradually shown that XBB is the dominant strain, mainly in terms of increased transmission and immune escape capacity. However, its pathogenicity is not significantly different from that of other Omicron strains, and there is no significant increase in severe disease and mortality rates in those countries where XBB is endemic. The study noted that the pathogenicity of XBB was not significantly increased, but that the infectivity of XBB.1.5 increased significantly due to the mutation of the strain to better bind to the human cell receptor.

At the same time, the recombinant strain XBB.1.5 is now the "latest version" of the new coronavirus, and our impression that antibody production by infection with other new coronaviruses is not effective has been confirmed by some studies. The results of the study showed that the antibodies in XBB.1 were not effective in people who had received three doses of the vaccine and were infected with strains BA.2 and BA.5.

The study showed that XBB.1 neutralization titers were not high in a population that had received three doses of vaccine and had been exposed to BA.2 and BA.5 strains. This means that a previous vaccination and a history of infection with a B family strain is not a good indicator for the new XBB series.

There is a very interesting phenomenon in immunology - immunological memory. Memory B cells are key players in this, and they are produced in the lymph nodes when the body is first exposed to a virus. These cells then watch for the same enemy in the bloodstream, ready to develop into plasma cells, which then produce antibodies in large numbers. The problem arises when the immune system encounters a similar but not identical strain of virus. In this case, the memory B cell response kicks in, rather than producing new B cells to produce tailored antibodies. This usually results in the production of old antibodies that combine features found in both old and new strains and are called cross-reactive antibodies. They may provide some protection, but are not perfectly suited to the new strain. Meanwhile, the cell paper vividly shows the complexity of the situation we are facing by the percentage of mutant strains from different regions, and by comparing the B family strains with the XBB family recombinant strains, we find that many monoclonal antibodies are directly ineffective against XBB and XBB.1, and that their immune escape is particularly pronounced, while at the same time their stinging proteins bind to ACE2 receptors no less well than the other new crown strains. This means that the XBB family as a whole is not less transmissible but has a gain in immune system attack that other strains do not have.





IV. Protection methods

Although more scientific studies are needed to support the data from the U.S. outbreak, there is no doubt that XBB.1.5 has a strong immune escape capability. If the XBB.1.5 virus were to spread in our country, it would trigger a second outbreak in the country. When facing XBB.1.5, we need to do some preparations.

1. Strengthen the statistics of the epidemic information

With the optimization of national epidemic control methods and the lifting of restrictions on nucleic acid testing in China, it is not easy to obtain accurate diagnostic results. If even XBB.1.5 is not clear, there is a risk of an outbreak. Nowadays, big data technology is highly advanced, and we need to have enough power to improve the quality of disease data.

2. Accelerate the development of new drugs

XBB.1.5 set a record average mortality rate of 1.524 per 100,000 people in the United States because Pfizer's new crown vaccine was not as effective as we thought it would be. To avoid a situation like the one in the United States in China, domestic research institutions should develop a new anti-Neo-Coronavirus drug in the shortest possible time, and its effectiveness should be better than that of Pfizer's effective drug.

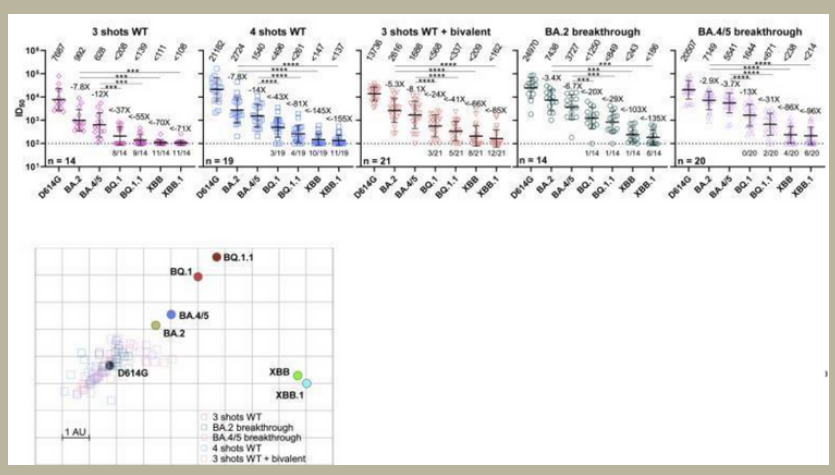
Personal protection is still necessary.

Even after recovering from a new coronavirus infection, you should still do an excellent job of personal protection; adhere to good living habits, regular work and rest, avoid staying up late, eat a sensible diet, drink moderately, eat more fresh vegetables and fruits, exercise moderately, and maintain a good attitude; reduce the number of gatherings, shorten the time of communities, and pass on blessings through video and telephone, mainly to avoid bringing the risk of infection to the elderly at home; strengthen health monitoring, and pay close attention to your health and that of your family. If you have symptoms such as fever, dry cough, weakness, sore throat, or positive nucleic acid or antigen test, stay in a well-ventilated and relatively independent room as much as possible, minimize contact with people living with you, closely monitor the progress of your illness, and seek medical attention if your condition worsens.

V. Summary

By 2023, XBB, XBB.1.5, and other new coronavirus variants will be the biggest and most difficult enemy to fight globally at this stage. With optimal epidemic control measures, human-virus symbiosis is inevitable, and there is nothing we can do to stop the virus, but we can use strategies to prevent them.

Lastly, We must not panic in the face of new challenges, but we must listen to both sides.

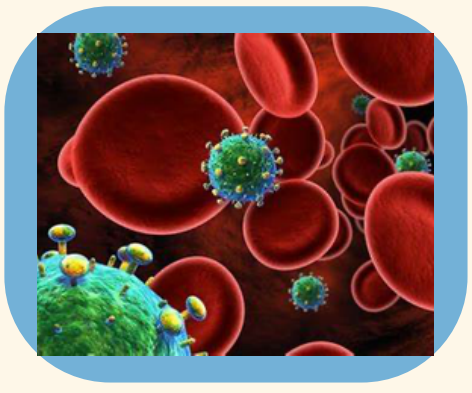


"With optimal epidemic control measures, human-virus symbiosis is inevitable, and there is nothing we can do to stop the virus, but we can use strategies to prevent them."

对于艾滋病感染者的一线新希望

S皮下注射：在皮下给药用药。
抗逆转录病毒药物：一类抑制逆转录病毒（如HIV）活性的药物。
Ryan White CARE 行动： 关于HIV的最重要的联邦计划。
RWHAP(Ryan White HIV/艾滋病 计划）为被诊断患有艾滋病的低收入人群提供艾滋病照护和治疗资金。

C病毒衣壳结构抑制剂：一类干扰艾滋病病毒衣壳结构的药物。
肌肉注射:一种将药物注入特定肌肉区域的注射。



介绍

人类免疫缺陷病毒(HIV)因其强烈地破坏你的免疫系统中的细胞，而削弱了你对抵抗日常感染和疾病的能力。AIDS（获得性免疫缺陷综合征）这个词指的是由HIV病毒严重破坏你的免疫系统引起的一系列可能危及生命的疾病。不能将AIDS从一个人传播到另一个人，但HIV病毒可以传播。

等等，HIV怎么做到的？

HIV目前尚无根治之法，但药物治疗非常有效，可以使大多数人保持健康和长寿。HIV治疗的目标是达到极少量的病毒残存量。这表明你体内HIV病毒的数量太低，无法通过检测识别出来。抗逆转录病毒药物是一种常见的治疗方法，根据世界卫生组织，它是一类抑制逆转录病毒（如HIV）发展的药物。这种药物通过阻止病毒在人体内的生长和复制，使免疫系统得以修复，从而避免进一步的伤害。有时HIV药物对某些感染群体不起作用，因为他们产生了耐药性，或药物治疗疾病或病情失去药效。这可能是由于HIV中的突变导致药物无法识别并抑制病毒在人体内的繁殖和传播。这些变化使之产生了一种新的抗药性病毒株，从而使许多HIV患者迅速对HIV药物产生耐药性。一项由旧金山艾滋病基金会发布的最新研究表明："超过70 - 80％的临床失败者患上了抗药性HIV感染（一旦一个人对其产生抑制，这些药物耐受性突变就不再是问题）（Wang Tong,2020）。"美国疾病控制与预防中心（CDC）的报告显示，大约44％的接受HIV治疗的患者无法实现病毒的抑制。

新药的研发...

此外，埃默里大学医学院的医学教授温迪·阿姆斯特朗（Wendy Armstrong）进一步指出，这种新的每年两次的药物也使面临出行困难的人们变得更加容易。这种治疗是有效的，但同时也非常昂贵。根据《今日美国》（USA Today）的报道，第一年治疗的费用为42,250美元，次年的费用为39,000美元。

幸运的是，瑞安·怀特护理法案（Ryan White CARE Act）和医疗补助（Medicaid）允许许多患者获得药物援助。与此同时，医疗界正在与政府联手，旨在尽快将药物添加到保险计划的处方中从药片到静脉注射，从每月至半年一次，医学的发展无疑大大改善了艾滋病患者的生活质量。目前尚无艾滋病的治愈方法，但是在治疗方面取得了巨大进步，专家希望扩大对长效药物的使用，将为更容易的治疗选择铺平道路。

总结与展望

我们在帮助患有艾滋病的人的同时也必须学会预防这种疾病。如果牢记下面的注意事项，可以大大减少暴露于病毒的风险。首先，在任何形式的性行为（口交、初次和肛交）中使用安全套至关重要。其次，不要共用针头或者其他注射器官，如注射器、勺子和棉签。第三，如果你可能接触到艾滋病毒，不要惊慌失措，应该在当地性健康诊所或全科医生那里寻求建议，了解如何最大限度地减少风险。患有艾滋病的人应该服用有效的抗艾滋病毒治疗药物，经常锻炼和保持健康的饮食习惯。

快来订阅SMART月刊吧！！！

HIV的新希望

written by: Sindy 何咏忻

Sunlence或lenacapavir是由吉利德科学公司开发，它是美国食品药物管理局（FDA）批准的新一类药物中的第一种，被称为顶体抑制剂。这些抑制剂通过抑制病毒的蛋白外壳或顶体来操作，中断病毒生命周期的许多阶段。根据ClinicalTrial.gov发表的一篇文章，83％的患者在近一年的时间里联合使用Sunlenca和其他HIV治疗方案，达到不可测病毒载量。治疗始安排于口服药物和注射剂，并维持六个月注射剂。波士顿医学中心的内科医生和传染病专家Sabrina Assoumou解释说，这种治疗对于在新冠爆发期间被确诊的老年患者特别有益，他们很难遵循以前更复杂的治疗方案，导致治疗产生耐药。

新的进展

很明显，开发对抗药性特别有效的新药物是非常重要的。去年早些时候，美国食品和药品监督管理局（FDA）批准由ViiV Healthcare公司每月或两个月一次注射的首个长效的肌肉内注射剂Cabenuva，用于治疗HIV/AIDS。发表在《新英格兰医学杂志》上的一项研究中，92.5％的参与者转换到Cabenuvamaintained不可检测的病毒负荷（少于50份/毫升）在48周（近一年）后，而95.5％继续其口服疗法。然而，由于注射频率的不便，副作用使得这种治疗方案不理想。2022年12月，Sunlence获得美国食品和药物管理局（FDA）的批准，是HIV医学治疗的里程碑，用于抑制已对其他疗法产生抗性的患者的HIV。注射频率也有所下降。

Hope for people living with HIV

written by: Sindy He

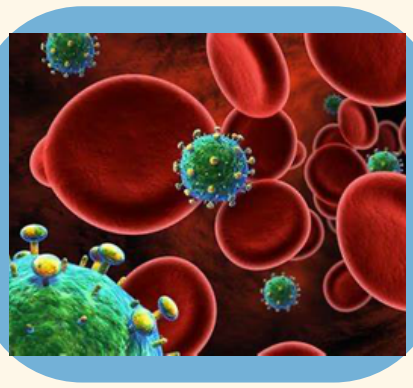
A new life jacket for people living with HIV

Subcutaneous administration: medication situated or applied under the skin.

Antiretroviral: a class of drugs that suppress the activity of retroviruses such as HIV. Ryan White CARE Act: The most significant federal program about HIV. The RWHAP (Ryan White HIV/AIDS Program) provides funding for HIV care and treatment for low-income people diagnosed with HIV.

Capsid inhibitors: A class of drugs that interfere with HIV capsid

Intramuscular injection: an injection which puts medications to a specific area of muscle.



What's more...

Additionally, Dr.Wendy Armstrong, a professor of medicine at Emory University School of Medicine, furthers that this new twice-yearly medication also makes it easier for people who face transportation difficulties. This treatment is effective and at the same time very expensive. According to USA Today, for the first year of therapy, the drug would cos t $42,250 , and for the following year, it would cost $39,000 a year.

Fortunately, the Ryan White CARE Act and Medicaid allows many patients to receive medication assistance . At the same time the medical profession is joining forces with the government aiming to have the drug quickly added to the formulary of insurance plans From pills to intra venous injections, from monthly to half-annually, developments in medicine have undoubtedly greatly improved the quality of life for HIV patients Th ere is no cure for HIV, but huge strides have been made in treatment, and experts hope that expanded access to long-acting drugs will pave the way for easier treatment options.

Summary

While we support people with HIV, we must also learn to prevent the disease. If you keep the following in mind, you can greatly avoid exposing to the virus. First and foremost, it is important to use a condom during any form of sexual activity (oral , virginal, and anal). Secondly, never share needles or other injection utensils such as syringes, spoons and cotton buds. Thirdly, if you may have exposed to HIV, do not panic, seek advice from your local sexual health clinic or GP on how best to reduce your risk. People living with HIV should take effective HIV treatment, exercise regularly and eat a healthy diet

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Introduction

The Human Immunodeficiency Viruses (HIV) weaken your ability to fight daily infections and illnesses because of its ability to damage the cells in your immune system aggressively. The term AIDS (acquired immune deficiency syndrome) refers to a wide range of potentially life-threatening diseases caused by the HIV virus severely damaging your immune system. There is no way to transmit AIDS from one person to another, but the HIV virus can.

Hold on, why can HIV do that?

HIV is not currently curable, but drug treatments are very effective at keeping most people healthy and long-lived. The objective of HIV therapy is to have a viral load that is unnoticeable. This indicates that the amount of HIV virus in your body is too low to be identified by a test. One common treatment is Antiretroviral medicines

which according to the World Health Organization is a class of drug that inhibits the development of retroviruses such as HIV. This drug works by preventing the virus from growing and duplicating in the human body, which enables the immune system to repair itself and consequently avoiding further harm. Sometimes HIV drugs do not work for some groups of infected people because they develop drug resistance, and loss of effectiveness of medication in treating disease or condition. This may be due to mutations in the HIV that cause the drug to fail to recognize and inhibit the virus from reproducing and spreading in the human body. These changes result in a new strain of virus that is resistant to the effect of the drug. Thus, many HIV patients develop resistance very quickly to HIV medicines. A recent study published by the San Francisco Aids Foundation states, "more than 70 - 80% of people with virological failure develop acquired HIV drug resistance. (Keep in mind that once a person becomes virally suppressed, these drug resistant mutations are no longer an issue) (Warren Tong, 2020)." Even more, the Federal Centers for Disease Control and Prevention, also known as CDC reports that approximately 44% of patients receiving HIV treatment have not been able to achieve viral suppression It is clear; it is important to develop new drugs that are particularly resistant to resistance.

Sunlence or lenacapavir is developed by Gilead Sciences. It is the first of a new category of drugs approved by the FDA known as capsid inhibitors. These inhibitors operate by inhibiting the virus's protein coat, or capsid, interrupting numerous phases of the viral life cycle. According to an article published by the ClinicalTrial.gov, 83% of patients who took Sunlenca with another HIV treatment combination reached an undetectable viral load after nearly a year. The therapy begins with a schedule of oral pills and injections, followed by six-month maintenance injections. A physician and infectious disease specialist at Boston Medical Center, Sabrina Assoumou, explains that this treatment may be particularly beneficial for elderly patients who are diagnosed during outbreaks of the COVID-19 and who have difficulty adhering to previously more complex treatment regimens, leading to treatment resistance

But what's New?

Earlier last year, the Food and Drug Administration (FDA) approved Cabenuva, the first longest-acting intramuscular injection given every month to two months by ViiV Healthcare company for the treatment of HIV/AIDS. In a study published in the New England Journal of Medicine, 92 .5% of participants switching to Cabenuva maintained undetectable viral loads (fewer than 50 copies/mL) after 48 weeks (almost a year), compared to 95.5% who continued their oral regimen. However, the side effects and the inconvenience due to the frequency of injections make this treatment option non-ideal. Sunlence, approved by the FDA in December, 2022, is a milestone for the medical treatment of HIV, and it is used to suppress HIV in patients who have become resistant to other regimens. The injection frequency also decreases.

Relation between COVID-19 and ACS

The sudden outbreak of the new coronavirus infection that caused a global pandemic caught people and healthcare systems off guard. As the virus was rapidly analyzed and tested, it was found that the main ways of transmission of SARS-Cov-2 is through respiratory droplets, aerosol transmission, infection vectors, and faecal-oral transmission. SARS-CoV-2 attaches to the target host cell angiotensin-converting enzyme-2 (ACE2) receptor, after which the virus is internalized and replicated. ACE2 receptors are highly expressed in upper and lower respiratory tract cells and mainly attack the respiratory tract and lungs (BMJ, n.d.). However, as research progressed, it was discovered that many patients did not die from respiratory distress syndrome and respiratory failure, but directly or indirectly from acute coronary syndrome (ACS). Although various types of lockdown measures and people's reduced activity due to fear of infection have led to a decrease in emergency department admissions. However, in cardiology, this has led to delays or non-admissions of cardiac patients. Most acute heart diseases require treatment as soon as possible, so this also indirectly led to an increase in the number of patients diagnosed with heart disease as the final cause of death during the COVID-19 pandemic (Cesaro et al. 2022).

On December 26, 2022, the author conducted research in multiple countries and regions such as Hong Kong, Japan, and the United States, and published an article entitled "How has COVID-19 impacted the care of patients with acute coronary syndromes?" in the journal Expert Review of Cardiovascular Therapy. Through quasi-quantitative research, the relationship between SARS-CoV-2 and ACS was revealed, and treatment duration and strategies for ACS were studied after restrictive measures were taken to control infection in cities. Additionally, the rates of various surgeries and bed turnover rates for ACS before and after the COVID-19 pandemic were compared.

The Direct Relationship Between The COVID-19 and Cardiovascular Disease

When we did meta-analysis for 1527 patients with COVID-19, at least 8% of patients had an acute myocardial injury, and the risk of severe clinical presentations was 13 times higher. The SARS-CoV-2 has an inflammatory and thrombotic effect, and it has been confirmed that it causes endothelial dysfunction and coagulation disorders. At the same time, the virus is also associated with coronary artery spasm, plaque rupture or thrombosis caused by systemic inflammation and cytokine storms, which will increase the likelihood of ACS in COVID-19 patients.

In addition, for patients diagnosed with ST-segment elevation myocardial infarction (STEMI), viral load, thrombus size, and thrombus burden are higher, and the prognosis is poor. 5%-25% of hospitalized patients with COVID-19 have increased cardiac troponin, and the increase in cardiac troponin is associated with a worse prognosis (Cesaro et al. 2022). In critically ill patients, infection-induced microvascular disease or hypercoagulable state can lead to thrombosis of capillaries, veins, and/or arteries, which may result in end-organ damage due to distant thrombosis or embolic disease (BMJ, n.d.).

Conclusion

Due to the reduction in PCI surgery for ACS and STEMI patients, and the delay of PCI surgery and NSTEMI patient care caused by the epidemic control, there has also been an increase in the number of deaths due to ischemic heart disease, 1.04 to 1.18 in the United States. The most important impact of COVID-19 infection on ACS patients is on the cardiovascular system rather than the respiratory system, and we need to take timely interventions to prevent deterioration such as heart failure. Therefore, the role of secondary prevention and treatment centres such as clinics is particularly important. They can provide early screening and basic treatment. At the same time, reasonable treatment paths should be developed to minimize the time for blood flow reconstruction.

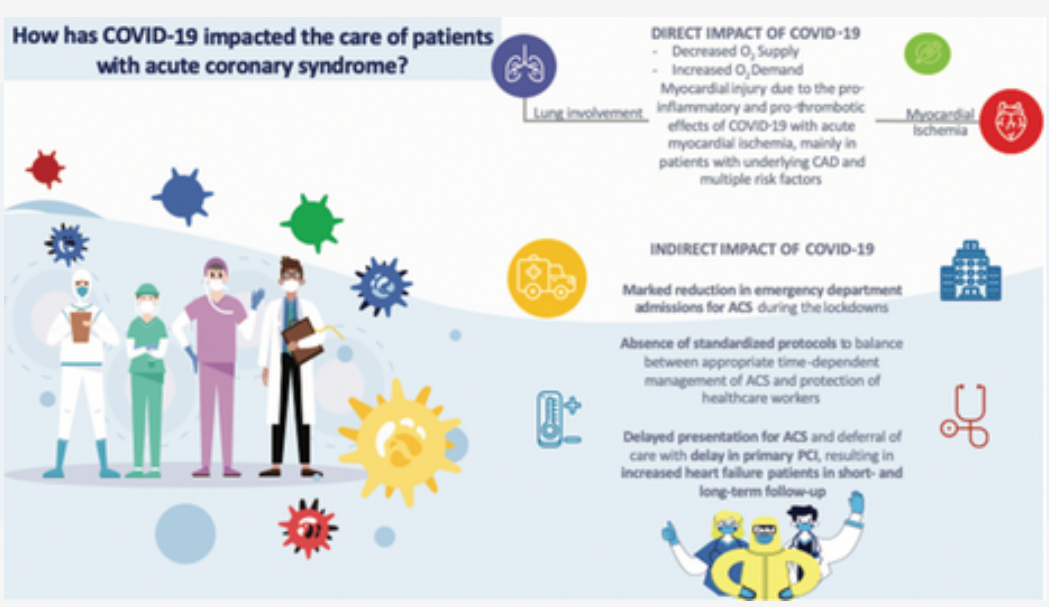


Figure 1. Direct and indirect impact of COVID-19 pandemic on care of patients with ACS.
ACS: Acute Coronary Syndrome. CAD: Coronary Artery Disease. COVID-19: Coronavirus disease 2019. PCI: Percutaneous Coronary Intervention.

新冠病毒与急性冠脉综合征的联系

突如其来的新型冠状病毒感染导致的全球大流行让全世界的人们及医疗系统措手不及。随着迅速的病毒分析与检验，我们发现新型冠状病毒SARS-Cov-2主要传播途径为呼吸道传播，气溶胶传播，传染媒介传播及粪口传播。SARS-CoV-2 附着于目标宿主细胞血管紧张素转化酶 2（angiotensin-converting enzyme-2, ACE2）受体，随后病毒被内化和复制。ACE2受体在上、下呼吸道细胞呈高度表达，主要攻击靶器官为呼吸道及肺部(BMJ，n.d.)。然而，随着研究的深入，我们发现许多患者并非死于呼吸窘迫综合征和呼吸衰竭，而是直接或间接的死于急性冠脉综合征（Acute coronary syndrome，ACS）。虽然各类封城措施以及人们因担心感染而减少出门导致急诊科入院人数减少，但是在心脏病领域，这却导致心脏病患者延迟或未入院。大多数急性心脏病需要在最短时间内的治疗，所以这也间接导致了新冠大流行期间因心脏病为最终死因诊断的患者人数上升(Cesaro et al. 2022)。

2022年12月26号，作者在香港，日本，美国等多个国家和地区展开研究并在Expert Review of Cardiovascular Therapy 发表了“How has COVID-19 impacted the care of patients with acute coronary syndromes?”一文。通过定量研究揭示了SARS-CoV-2与ACS之间的关系，在城市采取限制性措施控制感染后ACS的治疗时长及策略并且比较了新冠前后ACS的各类手术率和床位周转率。

新冠病毒导致心血管疾病的直接关系

当我们在对1527名新冠肺炎患者的数据进行的荟萃分析显示，至少8%的患者有急性心肌损伤，临床表现更严重的患者发生急性心肌损伤的风险高出13倍。新冠病毒有的促炎症和促血栓形成作用，现已被证实新冠病毒会导致内皮功能障碍和凝血障碍。同时，该病毒也与冠状动脉痉挛、斑块破裂或因全身炎症和细胞因子风暴而产生血栓有联系，这将导致新冠患者出现ACS的概率更高。此外，对于已经被诊断为ST段抬高型心肌梗死（STEMI）的患者，血栓病毒载量较高，血栓尺寸较高，血栓负担较高，预后较差。5%-25%的冠状病毒19型住院患者的心肌肌钙蛋白升高，肌钙蛋白的升高与预后恶化相关(Cesaro et al. 2022)。在重症患者中，感染引发的微血管病或高凝状态，导致毛细血管、静脉和/或动脉血栓形成，其可能由于远端血栓形成或栓塞性疾病导致终末器官损伤(BMJ，n.d.)。

新冠病毒与心血管疾病治疗的间接关系

由于出于对疫情的防控，在封控期间，医院及社会防疫政策，阻止了患者进入急诊科，这增加了从ACS症状出现到首次医疗接触的时间，导致治疗延期。在对2018年以及2020年（新冠流行期）STEMIT患者接受经皮冠状动脉介入治疗（Percutaneous coronary intervention，PCI）做比较发现，从症状发作到首次医疗接触的时间由82.5分钟延长至318分钟；从入院到导管室手术时间由84.5分钟延长至110分钟；从导管插入到支架展开时间由20.5分钟延长至33分钟。这表明医护人员需要更长的准备时间，因为防控疫情，需要额外穿戴个人防护设备。根据欧洲经皮心血管介入治疗协会，PCI仍然是STEMI和高风险非ST段抬高型心肌梗死（NSTEMI）患者的一线治疗手段而非溶栓治疗。在美国，于2019年同期相比，心血管重症监护室（CCU）床位占用率（4,8%）和床位周转率（50%）有所下降，但平均停留时间从3.26天增加到6.75天。在意大利，患者从进入手术中心到支架展开的时间超过了60分钟，较新冠流行前增加31.5%且进入手术中心到球囊展开时间的增加与住院死亡相关（OR 1.005，p=0.029）(Cesaro et al. 2022)。

结论

因为疫情封控导致ACS和STEMI患者PCI手术量的减少加上PCI手术的延迟和NSTEMI患者治疗护理的延迟，这也导致了因缺血性心脏病而去世的人数有所增加，如在美国为1.04至1.18。新冠感染对于ACS患者最重要的是心血管的影响而不是对于呼吸系统的影响，我们需要及时采取干预阻止恶化例如心力衰竭的发生。所以，二级预防治疗中心例如诊所的作用尤为重要。他们可以提供早期的筛查的基础的治疗。同时应制定合理的治疗路径，将血运重建的时间降到最短。

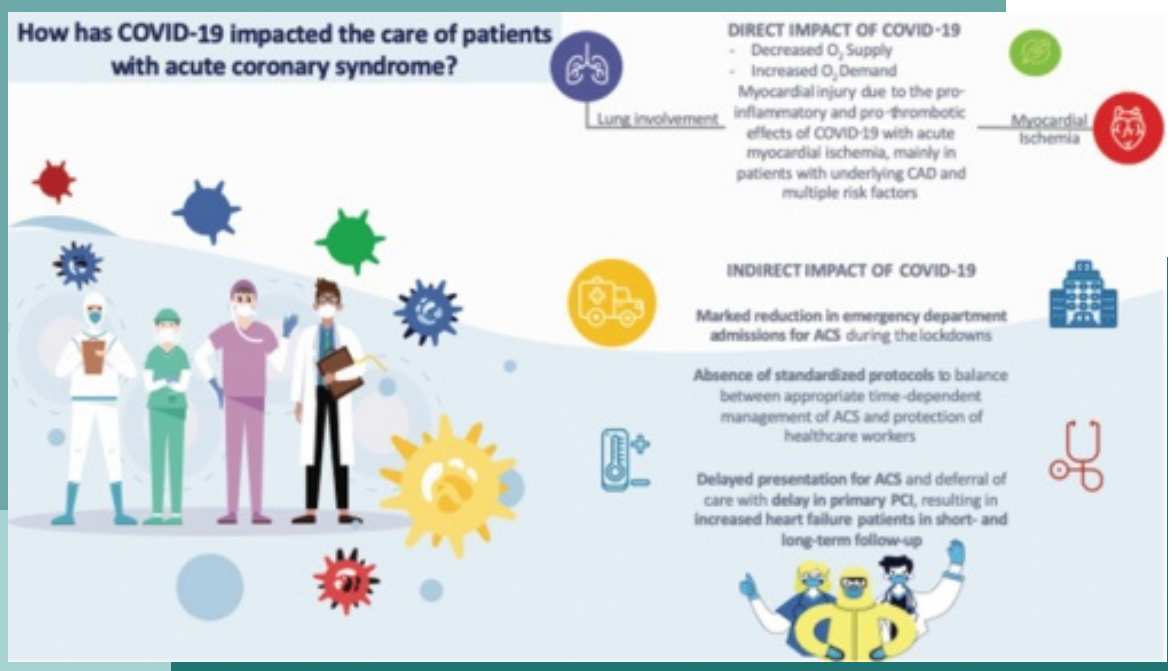
Relation between COVID-19 and ACS

Writer： Jan

The sudden outbreak of the new coronavirus infection that caused a global pandemic caught people and healthcare systems off guard. As the virus was rapidly analyzed and tested, it was found that the main ways of transmission of SARS-Cov-2 is through respiratory droplets, aerosol transmission, infection vectors, and faecal-oral transmission. SARS-CoV-2 attaches to the target host cell angiotensin-converting enzyme-2 (ACE2) receptor, after which the virus is internalized and replicated. ACE2 receptors are highly expressed in upper and lower respiratory tract cells and mainly attack the respiratory tract and lungs (BMJ, n.d.).

However, as research progressed, it was discovered that many patients did not die from respiratory distress syndrome and respiratory failure, but directly or indirectly from acute coronary syndrome (ACS). Although various types of lockdown measures and people's reduced activity due to fear of infection have led to a decrease in emergency department admissions. However, in cardiology, this has led to delays or non-admissions of cardiac patients. Most acute heart diseases require treatment as soon as possible, so this also indirectly led to an increase in the number of patients diagnosed with heart disease as the final cause of death during the COVID-19 pandemic (Cesaro et al. 2022).

On December 26, 2022, the author conducted research in multiple countries and regions such as Hong Kong, Japan, and the United States, and published an article entitled "How has COVID-19 impacted the care of patients with acute coronary syndromes?" in the journal Expert Review of Cardiovascular Therapy. Through quasi-quantitative research, the relationship between SARS-CoV-2 and ACS was revealed, and treatment duration and strategies for ACS were studied after restrictive measures were taken to control infection in cities. Additionally, the rates of various surgeries and bed turnover rates for ACS before and after the COVID-19 pandemic were compared.



The direct relationship between the COVID-19 and cardiovascular disease

When we did meta-analysis for 1527 patients with COVID-19, at least 8% of patients had an acute myocardial injury, and the risk of severe clinical presentations was 13 times higher. The SARS-CoV-2 has an inflammatory and thrombotic effect, and it has been confirmed that it causes endothelial dysfunction and coagulation disorders. At the same time, the virus is also associated with coronary artery spasm, plaque rupture or thrombosis caused by systemic inflammation and cytokine storms, which will increase the likelihood of ACS in COVID-19 patients.

In addition, for patients diagnosed with ST-segment elevation myocardial infarction (STEMI), viral load, thrombus size, and thrombus burden are higher, and the prognosis is poor. 5%-25% of hospitalized patients with COVID-19 have increased cardiac troponin, and the increase in cardiac troponin is associated with a worse prognosis (Cesaro et al. 2022). In critically ill patients, infection-induced microvascular disease or hypercoagulable state can lead to thrombosis of capillaries, veins, and/or arteries, which may result in end-organ damage due to distant thrombosis or embolic disease (BMJ, n.d.).

Indirect relationship between COVID-19 and treatment of cardiovascular disease

Due to the control of the epidemic, during the period of lockdown/circuit-breaker, due to hospital and social epidemic prevention policies, patients were hindered from entering the emergency department which increased the time from the onset of ACS symptoms to the first medical contact, resulting in delayed treatment. Comparing STEMI patients who underwent percutaneous coronary intervention (P in 2018 and 2020 (during the COVID-19 pandemic), the time from symptom onset to first medical cont increased from 82.5 minutes to 318 minutes; the time from hospital admission to catheterization laboratory surgery increased from 84.5 minutes to 110 minutes; and the time from catheter insertion stent expansion increased from 20.5 minutes to 33 minutes. This indicates that healthcare workers ne more preparation time due to the epidemic control and the need to wear additional personal protecti equipment

According to the European Society of Cardiology, PCI remains the first-line treatment for STEMI and hi risk non-ST elevation myocardial infarction (NSTEMI) patients, rather than thrombolysis. In the United States, compared to the same period in 2019, the occupancy rate (4.8%) and bed turnover rate (50%) o the cardiovascular intensive care unit (CCU) decreased, but the average length of stay increased from 3.26 days to 6.75 days. In Italy, the time from entering the surgical centre to stent expansion exceeded minutes, an increase of 31.5% compared to before the COVID-19 pandemic, and the increase in time from entering the surgical centre to balloon expansion was related to inpatient mortality (OR 1.005, p=0.029) (Cesaro et al. 2022).

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Figure 1. Direct and indirect impact of COVID-19 pandemic on care of patients with ACS.
ACS: Acute Coronary Syndrome. CAD: Coronary Artery Disease. COVID-19: Coronavirus disease 2019. PCI: Percutaneous Coronary Intervention.

Conclusion

Due to the reduction in PCI surgery for ACS and STEMI patients, and the delay of PCI surgery and NSTEMI patient care caused by the epidemic control, there has als been an increase in the number of deaths due to ischemic heart disease, 1.04 to 1.18 in the United States. The most important impact of COVID-19 infection on ACS patients is on the cardiovascular system rather than the respiratory system, and w need to take timely interventions to prevent deterioration such as heart failure. Therefore, the role of secondary prevention and treatment centres such as clinics i particularly important. They can provide early screening and basic treatment. At th same time, reasonable treatment paths should be developed to minimize the time for blood flow reconstruction.

Abstract

The new policy for COVID was implemented in our country and many people developed and even died from pneumonia caused because of it. One of the many types of pneumonia described in this article is ----- Community Acquired Pneumonia（CAP).

One of types of pneumonia ----- Community-acquired pneumonia (CAP) refers to infectious parenchymal inflammation (CAP) that occurs outside the hospital, including pneumonia that develops within 48 hours of a patient's admission to hospital from a pathogen with a defined incubation period. With an ageing population, antibiotic overuse and pathogens with drug resistance, new challenges is faced in the prevention and treatment of CAP. However, new antibiotics and gene

sequencing technologies are also offering the promise of reducing mortality. This article will only focus on the pathological causes of CAP to provide an understanding of the underlying mechanisms behind it. The underlying mechanisms can be summarised in two main points: 1. immune response triggered by the invasion of pathogens into the body 2. genetic changes that lead to an increased susceptibility to CAP. Therefore, research into the genetic variation of CAP is valuable in furthering our understanding of the pathogenesis of CAP. However, most of them have not been studied and need to be further investigated. It is hopeful to be used in the future to prevent CAP or to reduce CAP mortality.

PATHOLOGY OF COMMUNITY-ACQUIRED PNEUMONIA

keywords：
immune response
cytokines genes
mutation

Point 1 immune response leading by pathogens

Community-acquired pneumonia(CAP) is an infectious inflammation of the lung parenchyma that develops outside the hospital, including pneumonia that develops within 48 hours of a patient's admission to hospital from a pathogenic infection with a defined incubation period. It is a common infectious disease of the lower respiratory tract with a high incidence and burden of disease, high rates of death and treatment failure increaseing with the age of the patient. One of the pathological causes is a variety of pathogens such as bacteria such as Streptococcus pneumoniae, Staphylococcus aureus, Mycoplasma pneumoniae and Gram-negative enterobacteria, fungi such as Histoplasma, Bacillus and Coccidioides or viruses such as influenza virus and adenovirus.

The lower respiratory tract is usually reached by four mechanisms: 1. inhalation of diseased aerosols 2. inadvertent aspiration of oropharyngeal secretions into the trachea and entry into the lower airways via the trachea 3. blood-borne transmission from a locally infected site 4. direct spread of nearby infected lesions. The pathogen invades and overgrows in the lung parenchyma, which exceeds the host's defence limits and causes exudate to develop in the alveolar cavity. Normally, in the body's defence system, the immune response is triggered when foreign unrecognisable agents are encountered. The foreign cells release chemical factors and the white blood cells are the first to reach the pathogen and engulf it and signal more white blood cells to kill the pathogen. But it is the immune response of the leukocytes that leads to the outcome in pneumonia. A type of leukocyte ---- mast cell releases cytokines which cause the blood vessels to dilate and become more permeable, as more fluid will facilitate the leukocytes to kill the pathogens, but this also creates a build-up of fluid in the lungs. Similarly, an increase in temperature, for example, is beneficial to the white blood cells in their fight which will increase the inefficiency. Also, like coughing is designed to drive pathogens out of the body to protect our body.

Point 2 gene mutations

Scientists have also discovered that the pathology of CAP is genetically related through techniques such as Luminex. The influence of CAP. In the respiratory tract, motile cilia are responsible for the removal of mucus, thereby protecting it from infection and ensuring mucociliary clearance.

Some scientists have identified genes such as ARMC4 as playing an important role in ciliary motility in anchoring the outer dynein arms. In defective cases, affected cilia exhibit reduced beating frequency and amplitude or become immobile, and malfunctions in the coordinated movement of cilia can impede the clearance of invading microorganisms from the airways and promote respiratory infections.

As a result, patients with autosomal recessive disorders like primary ciliary dyskinesia often develop recurrent pneumonia. Scientists have found that the 250-base ACE gene is also associated with CAP, and elderly patients from long-term care facilities who carry a pure combination of this gene are more likely to develop pneumonia over eight months (excluding winter). Several recent prospective longitudinal observational studies have shown that the use of ACE inhibitors is associated with a lower incidence of pneumonia. Variants in TLR4 a gene that identifies the molecule, appear to increase the risk of severe Gram-negative infection to trigger CAP.

A cytokine called Tumor Necrosis Factor (TNF) is critical to the immune response to infection, and experimental animals who lack TNF could not survive in the challenge of infection. The A allele of TNF-308 is associated with an increased risk of multiple infectious diseases

Further understanding of the pathogenesis of CAP would be valuable through the study of CAP gene variants. Many other cytokines and chemokines are important in the immune response to infection, but most have not been well studied and require further research.

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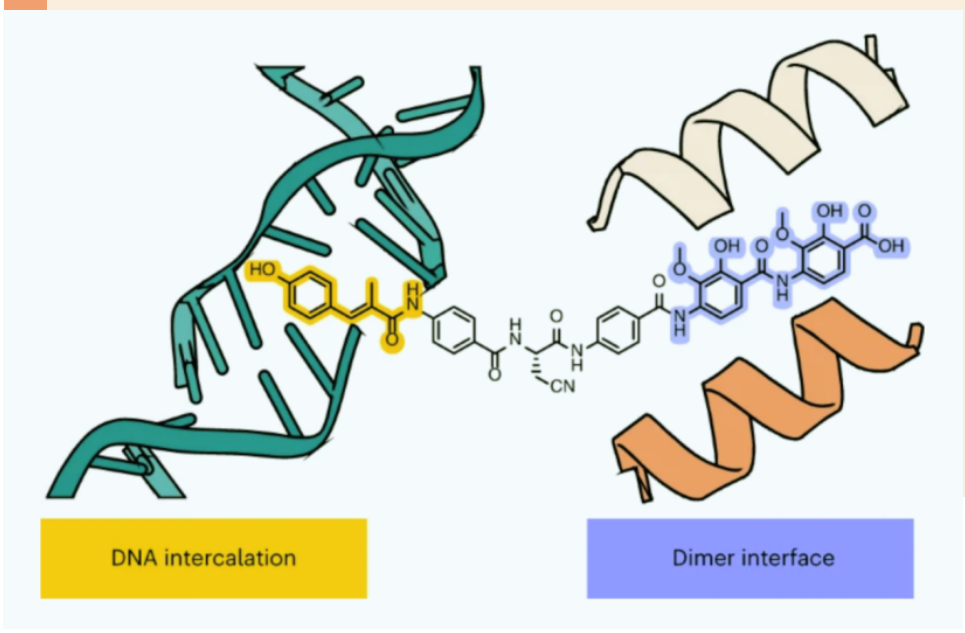
肽致拓扑异构酶中毒的分子机制

关键词

白霉素
DNA拓扑异构酶抑制剂
双结合机制
低温电镜结构



背景

目前，科学界迫切需要一种新型抗革兰氏阴性细菌药物——也是本研究的背景。
源于医院的革兰氏阴性细菌造成了很高的死亡率，且变得越来越耐药。然而，在过去的50年里，还没有发现针对革兰氏阴性细菌的新类别。在临床前试验中，候选药物的消耗率很高，这意味着来自革兰氏阴性细菌的挑战降低了这些候选药物的强度。

目前有许多候选抗生素和正在使用的抗生素，它们通常有一个共同的原理：细菌II型拓扑异构酶DNA旋回酶，以及同源拓扑异构酶IV (Topo IV)对细菌是必需的，但在人体中不存在，这也使得它们成为抗生素的主要靶标。DNA旋回酶由两个GyrA和两个GyrB单体组成。它负超缠绕DNA:在结合段(G或门段)使用临时双链断裂，同一DNA的相邻(T或运输)段被引导通过G段，在这个过程中消耗ATP。

目前针对革兰氏阴性菌的可能解决方案包括以下几种。首先，F1旋回酶中毒机制利用插层进入裂解的DNA形成fq蛋白-DNA复合物，导致细胞死亡。然而，这个方案有严重的副作用，所以目前在美国被一个黑框警告限制使用。第二种是使用“新型细菌拓扑异构酶抑制剂”(NBTIs)，如gepotidacin，来模拟FQs的有效过程。目前正在进行III期试验，虽然NBTIs通常具有心脏毒性，但gepotidacin本身对心率的影响很小。最后一个方案是正在研究的:白壁素。它是由白色白单胞菌(Xanthomonas albilineans)产生的，这种细菌会导致甘蔗叶片烫伤。它能在纳摩尔浓度下抑制DNA旋回酶，其衍生物具有较高的有效性和良好的安全性。该白菌素由6个残基组成:甲基对香豆酸(MCA1)、对氨基苯甲酸(pABA2和pABA4)、β-氰基-l-丙氨酸(Cya3)和4-氨基-2-羟基-3-甲氧基苯甲酸(pMBA5和pMBA6)。

实验

首先，研究小组测试了白壁素稳定裂解复合物的要求。DNA旋回酶使用旋回酶裂解核融合，这是一种截断和融合的结构。它由GyrB单体c端拓扑异构酶引物酶(TOPRIM)结构域和GyrA单体n端部分组成。根据以往的经验，研究小组假设白壁素结合需要DNA链传代事件。由于microcin(一种抗生素肽)B17稳定旋回酶裂解复合体需要很长的DNA片段，他们预计稳定旋回酶裂解复合体也需要同样的稳定要求，并测试了一系列具有噬菌体Mu强旋回结合位点(SGSs)的不同DNA片段。他们发现，在白霉素和ATP或类似物ADPNP存在的情况下，217 bp Mu SGS片段(Mu217)发生了强烈的裂解，不能被水解。

此外，他们还发现，在小于150 bp的DNA链或缺乏核苷酸的情况下，几乎没有检测到卵裂，这意味着可以与GyrA CTD结合的长DNA片段的存在对卵裂至关重要。此外，核苷酸的存在和DNA底物的长度共同使裂解复合体稳定。由于Mu217能够被裂解，他们扩大了该碎片的产量，用于后续阶段的结构测定。

随后，研究小组确定了白壁素捕获DNA旋回酶的具体机制。与ATP同源物ADPNP的旋回酶-DNA-白壁素复合物表现出高度的结构同质性，几乎没有DNA静态紊乱。这使得解理核的结构可以在2.6Å的局部分辨率下确定。数据的清晰度比以前有了很大的提高。我们也看到了包裹DNA的GyrA的CTD和属于GyrB的atp酶，但由于结构固有的灵活性，分辨率较低，因此没有建模。复合物的整体结构类似于gyrase和前面提到的NBTI gepotidacin之间的结构，除了预期的DNA和DNA片段在该位点的裂解外，几乎完全对称。

结果

首先，白菌素的n端插入，也就是说，插入到两条DNA链之间。n端(MCA1)插入在FQ的确切裂解位点5 ' -T/ gatt -3 '，尽管机制不同，而MCA的末端羟基在相应的C/A到达相反的链上。第二，在另一端，c端，同样插入α3和α3'之间，两个相反的螺旋。这使得GyrA/GyrA的界面得以形成。第三，在GyrA/GyrA的界面上有显著的大小变化，其特征是滑动门运动。在GyrB和DNA末端也出现了类似的显著变化。结果是，催化中间状态类似于部分开放和完全开放之间的状态。第四，前面提到的白霉素的n端，只占据了一半的裂解位点(也称为TG口袋)。这导致了对称相关的AA口袋中DNA的明显扭曲，使TG口袋具有很强的选择性。第五，白壁素的pMBA5和pMBA6以伪对称的方式结合，占据GyrA和GyrA '中的疏水口袋。第六，他们使用白菌素的光交联(能够形成光诱导共价键)类似物来确定白菌素的结合模式。他们发现，白壁素n端与裂解DNA相互作用都需要旋回酶和催化条件。第七，确定了Topo IV对应物II型拓扑异构酶对金属离子依赖性DNA的切割机制。在这里，离子基本上被确定为Mg2+。金属离子依赖性的DNA裂解活性可能是:在链传代过程中，使用B构型暂时储存金属，然后镁离子始终附着在Asp500残基上。尽管在DNA降解之前(断裂后DNA片段的结合)招募第二个离子，这一过程也可能发生。

此外，增强白菌素衍生物被用来显示结合的异质性。首先，Albi-1是一种衍生物，对fq耐药病原体表现出更高的药理学特征和纳摩尔范围的活性。对该导数的初步分析表明，该结构中存在三个阶段。这可能是由于Albi-1的n端较短，允许TG和AA口袋同时占据。其次，去除pMBA6的c端截断导数显示活性下降，这表明pMBA5和pMBA6对捕获旋回酶都很重要。第三，他们测试了Albi-2和Albi-3衍生物，其中MCA1被同样能够插入DNA的等价物所取代。对于Albi-2，在旋回酶抑制方面比Albi-3有四倍的活性。

除此之外，位点定向诱变也证实了之前确定的白壁素的结合方式。该团队使用ConSurf服务器提供的GyrA亚基的多个序列比对，以防止人为设计的突变产生非自然的替换。他们通过检查产生的变异和原始的白霉素发现:首先，结合几乎完全不受GyrA喹诺酮耐药决定区(QRDR)突变的影响。其次，尽管GyrB QRDR中的Lys447突变提供了一些抗性，特别是对母体化合物的抗性，但正如Albi-3所证明的那样，它的影响可以通过dna插层部分的改变成功克服。第三，GyrAA67Q突变提供了一些对Albi-1或Albi-3的抗性，但它不太可能自然发生，因为它破坏了gyrase功能。
最后，确定白菌素的靶向特异性。研究小组最初怀疑是Topo IV和gyrase的双重靶点。除Albi-2外，Albicidin衍生物均能稳定与Topo IV的裂解，但Albi-1性能最好。Albi-1和Albi-3的抑制作用只需要其他衍生物的1/10浓度。在任何情况下，albicidin都可以抑制Topo IV，虽然抑制效率低于gyrase，但进一步修饰可以提高抑制效率。

总结

总之，本研究提供了基于结构的设计，保留了白细胞白素独特而有效的抑制机制。Albi-1和Albi-3在动物模型中表现出安全性和有效性。α3/α3'口袋是独特的，不与其他类型的抑制剂重叠。Albi-1和Albi-3在解理配合物稳定方面具有纳摩尔活性，比NBTIs更强，且解理配合物比例高。白壁素靶向Topo IV和gyrase，使耐药性更难产生。电流衍生品的活度较低，但可以提高。未来，为了成功的临床应用，需要增加溶解性、血浆稳定性和血浆蛋白结合，同时监测对真核拓扑异构酶II的毒性。对我们生命的意义。
蛋白酶是生物体内重要的大分子物质。本文所讨论的肽类抗生素在临床治疗中具有重要意义。研究其抑制DNA旋回酶的机制对于这种抗生素的当前和未来的应用非常重要，与我们的生活密切相关。

引用本文

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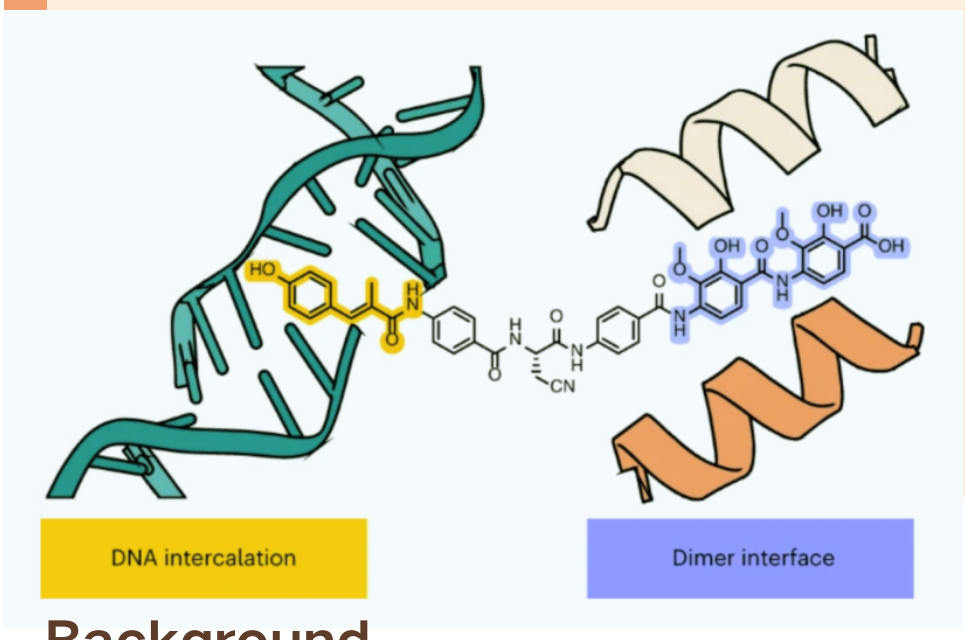
Key Words

albicidin
DNA topoisomerase inhibitor
dual binding mechanism
cryo-EM structure

Molecular mechanism of topoisomerase poisoning by the peptide antibiotic albicidin



Background

Currently, there’s an urgent need for a new class effective against Gram-negative bacteria. This is the background of this research. Gram-negative bacteria originating in hospitals cause a high death toll, and are becoming more pan-resistant. However, there hasn’t been a new class discovered targeting Gram-negative bacteria in the last 50 years, and there has been high attrition rates of drug candidates in preclinical trials, meaning that challenges from Gram-negative bacteria reduces the strength of these candidates.

There currently exist many candidates and in-use antibiotics, and they often share a common principle. The bacterial type II topoisomerase DNA gyrase, along with the homologous topoisomerase IV (Topo IV) are essential for bacteria but absent in humans, making them main targets in antibiotics. The DNA gyrase is made up of two GyrA and two GyrB monomers. It negatively supercoils DNA: this uses a temporary double-strand break in the bound segment (G or gate segment) and the adjacent (T or transported) segment of the same DNA is guided through the G segment, in a process that consumes ATP.

Current possible solutions for Gram-negative bacteria include the following. First, the F1 gyrase poisoning mechanism uses intercalating into cleaved DNA to form the FQ-protein-DNA complex, leading to cell death. However, this option has severe side-effects, so is currently restricted use by a black box warning in the US. Second is using ‘novel bacterial topoisomerase inhibitors’ (NBTIs), such as gepotidacin, to mimic the effective process of FQs. This is currently under phase III trials, and though NBTIs usually are cardiotoxic, gepotidacin itself only has a mild effect on heart rate. The final option is the one under investigation: albicidin. It’s produced by Xanthomonas albilineans, a bacteria that causes leaf scald disease in sugarcane. It inhibits DNA gyrase at nanomolar concentration, and has derivatives with higher effectivity and good safety profile. This albicidin is made up of six residues: methyl p-coumaric acid (MCA1), p-aminobenzoic acid (pABA2 and pABA4), β-cyano-L-alanine (Cya3) and 4-amino-2-hydroxy-3-methoxybenzoic acid (pMBA5 and pMBA6).

实验

To start with, the team tested for requirements of the stabilization of the cleavage complex by albicidin. DNA gyrase uses gyrase cleavage core fusion, which is a truncated and fused structure. It’s made up of C-terminal topoisomerase-primase (TOPRIM) domain of GyrB monomer and N-terminal part of GyrA monomer. From previous experience, the team hypothesized that the albicidin binding requires a DNA strand passage event. Because the stabilization of gyrase cleavage complex by microcin (an antibiotic peptide) B17 requires a long DNA segment, they expected the same stabilization requirement to be true for the stabilization of the gyrase cleavage complex, and tested a range of different DNA fragments with strong gyrase-binding sites (SGSs) of phage Mu. They found that strong cleavage of the 217 bp Mu SGS fragment (Mu217) occurs in the presence of albicidin and ATP or the analogue ADPNP, which could not be hydrolysed. Also, they made the important discovery that almost no cleavage was detected in the presence of less than 150 bp DNA strand or in the absence of nucleotide, meaning that the presence of a long DNA fragment, which can bind to GyrA CTD was essential for cleavage. Further, the presence of the nucleotide and the length of the DNA substrate collectively enabled the cleavage complex stabilization. Since Mu217 was able to be cleaved, they scaled up production of the fragment for use of structure determination in the following stages.

Following that, the team determined the specific mechanism through which albicidin traps DNA gyrase. The gyrase-DNA-albicidin complex with the ATP homologue ADPNP exhibited high structural homogeneity and virtually no DNA static disorder. This enabled the structure of the cleavage core to be determined at local resolution of 2.6Å. The clarity of the data was a significant improvement from previous ones. The CTD of GyrA with wrapped DNA and the ATPase belonging to GyrB were also seen, though at lower resolution due to intrinsic flexibility of structure, and so were not modeled. The overall structure of the complex resembles that between gyrase and the aforementioned NBTI gepotidacin, with almost perfect symmetry except the DNA and cleavage of the DNA fragment at the site expected.

Result

First, the N-terminal of albicidin intercalates, that is to say, inserts between the two strands of the DNA. The N-terminal (MCA1) insertion was at the cleave site, 5’-T/GATTT-3’, the exact cleave site for FQ, though with differing mechanisms, while the terminal hydroxyl of the MCA reached the opposite strand at the corresponding C/A. Second, at the opposite end, the C-terminal, similarly inserted between the α3 and α3’, two opposing helices. This allowed the formation of the GyrA/GyrA’ interface. Third, there’s significant sized shifts at the GyrA/GyrA’ interface, characterized by a sliding door motion. Similar significant shifts were also present in GyrB and at the DNA ends. The result was that the catalytic intermediate state resembles a state between being partially open and fully open. Fourth, the aforementioned N-terminal of albicidin, only occupied half of the cleavage site (also called the TG pocket). This led to pronounced distortion of DNA in the symmetrically-related AA pocket, enabling strong selectivity for the TG pocket. Fifth, the pMBA5 and pMBA6 of albicidin bound in a pseudosymmetric manner, occupying the hydrophobic pockets in GyrA and GyrA’. Sixth, they used the photocrosslinkable (able to form a photo-induced covalent bond) analogue of albicidin to determine the binding mode of albicidin. They found that gyrase and the catalytic conditions were both needed for the N-terminus of albicidin to interact with cleaved DNA. Seventh, the mechanism of the metal-ion dependent DNA cleavage by the Topo IV counterpart–type II topoisomerase–was determined. Here, the ion was largely ascertained to be Mg2+. The activity of metal-ion dependent DNA cleavage may be as follows: the B configuration was used to store the metal temporarily during the strand passage event, then the magnesium ion remained attached to residues Asp500 throughout. Though the recruitment of a second ion before DNA relegation (joining of DNA fragments after breakage), which this process occurs, is also possible.

Moreover, the potentiated albicidin derivatives were used to show binding heterogeneity. First, Albi-1 is a derivative that exhibits higher pharmacological characteristics and nanomolar-range activity toward FQ-resistant pathogens. Initially, analysis of this derivative showed three stages coexisting in the structure. This was possibly due to the shorter N-terminal of Albi-1, which allowed both TG and AA pocket occupation. Second, the C-terminally truncated derivative, where pMBA6 was removed, shows a decrease in activity, suggesting that both pMBA5 and pMBA6 were important for trapping gyrase. Third, they tested the Albi-2 and Albi-3 derivatives, where MCA1 was replaced by equivalents that were also able to intercalate in DNA. For Albi-2, there’s a four time better activity in terms of gyrase inhibition compared to Albi-3.

Besides this, the site directed mutagenesis also confirmed the previously determined binding mode of albicidin. The team used multiple sequence alignment of GyrA subunits provided by the ConSurf server to prevent artificially designed mutations from creating unnatural substitutions. They found the following through examining the resulting variants and the original albicidin: First, binding was almost completely unaffected by mutations in the quinolone-resistance determining region (QRDR) of GyrA. Second, though the Lys447 mutation in GyrB QRDR offered some resistance, especially to the parent compound, its effect could be successfully overcome by the alterations of the DNA-intercalating moiety as demonstrated by Albi-3. Third, the GyrAA67Q mutation provided some resistance to Albi-1 or Albi-3, but it was not likely to naturally occur because it disrupted the gyrase function.

Finally, the target specificity of albicidin is determined. The team initially suspects a dual-target of Topo IV and gyrase. Albicidin derivatives can all stabilize cleavage with Topo IV, except Albi-2, though Albi-1 has best performance. Albi-1 and Albi-3 for inhibition require only 1/10 the concentration of the rest of the derivatives. In any case, albicidin can inhibit Topo IV, though with lower efficiency than with gyrase, but further modifications can increase the efficiency

Discussion

As a conclusion, this research provides structure-based design that preserves albicidin’s distinct and potent inhibition mechanism. Albi-1 and Albi-3 show safety and efficacy in animal models. The α3/α3’ pocket is unique and doesn’t overlap with other classes of inhibitors. Albi-1 and Albi-3 have nanomolar activity in cleavage complex stabilization, which is more potent than NBTIs, as well as a high proportion of cleaved complexes. Albicidin targets Topo IV and gyrase, making resistance harder to develop. Activity of current derivatives is lower, but can be improved. In the future, for successful clinical application of albicidins, solubility, plasma stability, and plasma-protein binding need to be increased, while monitoring the toxicity to eukaryotic topoisomerase II.

The significance to our life

Protease is an important macromolecular substance in living organisms. The peptide antibiotics discussed in this paper are of great significance in clinical treatment. The research on the mechanism of its inhibition of DNA gyrase is very important for the current and future applications of this antibiotic, are closely related to our lives.

Citations

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主题词： 肠道; 环境污染物; 修复

环境污染物和肠道健康

作者：Polaris

背景

在过去，很多学者已经对环境污染物展开了各类研究，传统污染物大致包括多氯联苯（PCB）、农药、重金属和工业污染物，然而随着工业化和资源开采的加剧，新型污染物主要包括全氟烷基物质，微塑料，持久性有机污染物，二恶英类化合物，纳米材料、药物、人造甜味剂等。

大多数新型污染物没有相关政策限制，可能意味着具有很大的潜在致病隐患。尤其是近年来，越来越多的研究发现污染物不再局限于大气中存在，在土壤和水资源中也被检测到。因此，污染物在食物链中积聚并转移到人体。

肠道是人体抵御外来物质的第一道屏障。肠道屏障与环境污染物的存在密切相关。有研究提出环境污染物通过诱导氧化应激和改变肠道微生物群等损伤肠道屏障，因而导致疾病。此外，已经证明肠道细菌可能具有降解体内污染物的效果，并且一些保护肠道健康的物质在促进污染物从体内排泄方面发挥作用。为了解决环境污染物造成的肠道健康问题，本文基于已有文献的基础上整理了一部分较有代表性的肠道影响，并以此为切入点探索了两个层面上缓解环境污染物造成的影响的方法。

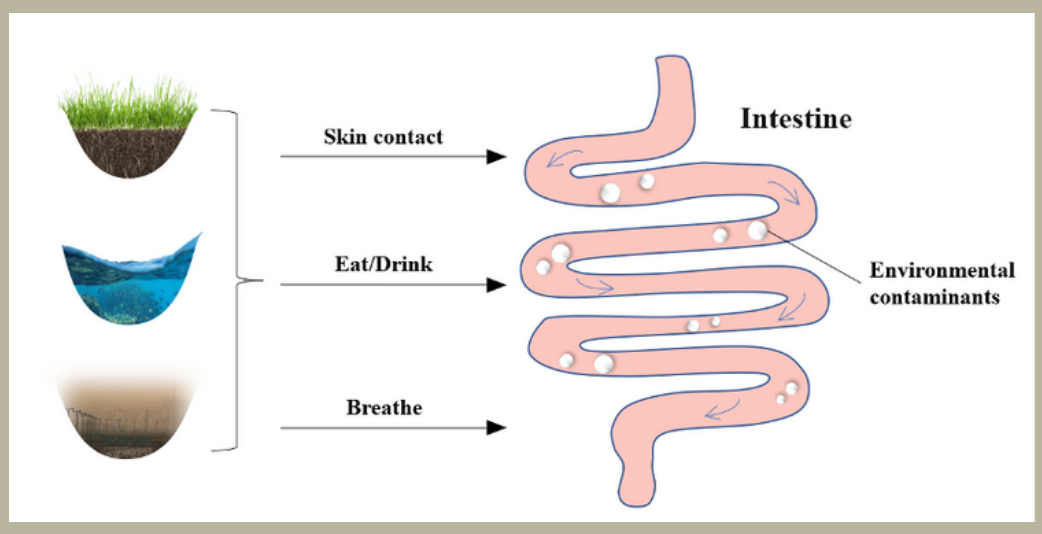
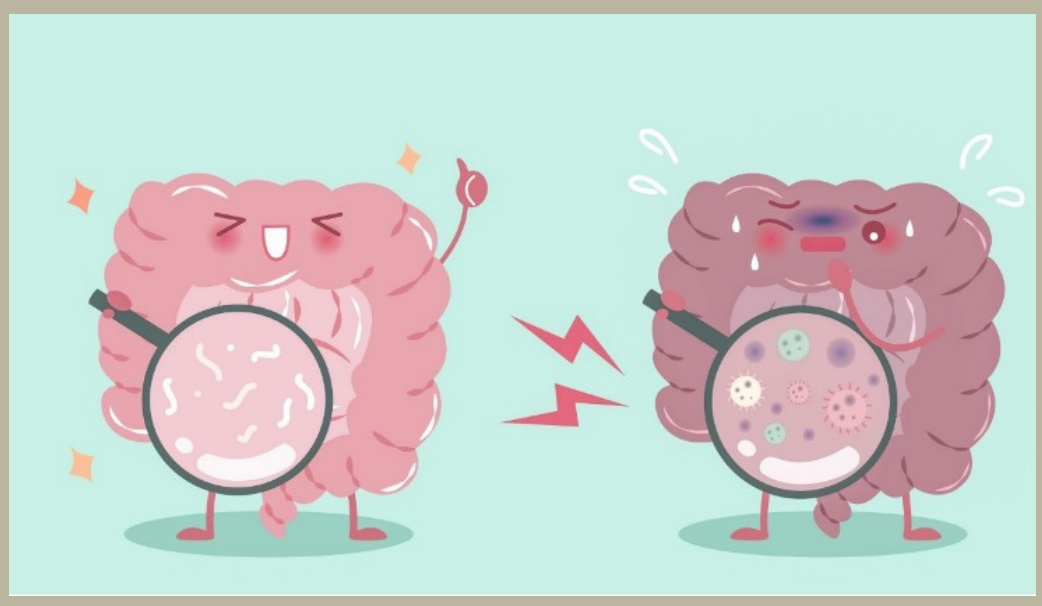


图1：环境污染物的迁移。

缓解环境污染物对肠道造成的影响

药物（比如抗生素）对减少体内污染物的同时往往带来一定的副作用。饮食调整成为了维持肠道健康的常用手段。益生菌，益生元等具有肠道稳定性和多种功能活性的功能食品是市场上较为成熟的调整肠道稳态失调的产品。海藻多糖（一种益生元）被证明可以有效调整肠道菌群的失调。多种益生菌的混合物被报道可以抑制致病菌(肠杆菌)的生长和增加厚壁菌。在细胞和动物实验中，具有调控紧密连接蛋白和增加有益细菌的丰度作用的草本提取物也可以实现调节人体微生物群的平衡的目的。很多学者发现，一些动物的肠道菌群中提取出的菌株对MPs存在一定降解的作用。蚯蚓肠道中的细菌可以减小MPs的大小。从蜡蛾的肠道提取的肠杆菌属菌株可以降解微塑料。根据已有的报道，我们可以发现达到肠道屏障修复效果的成分，大多是活性物质且具有一定的抗菌作用，这对未来筛选高效缓解肠道屏障损伤的物质提供了新的思路



讨论

环境污染物损伤肠道屏障

相比人们对重金属的相关研究，目前环境中出现的新型污染物对肠道的研究得到了更多的重视。本文选取了较有代表的新型污染物，微塑料（MPs）。过去的一项研究表明，全球海面上浮动的塑料颗粒大约有268，940吨， 5.25万亿个塑料颗粒。MPs显著降低了跳尾部肠道的细菌多样性。土壤中，国内有研究发现塑料残留物积累已达550,800吨。多项研究中发现，在空气，食物，日用品和水供应中都检测到了MPs，这可能意味着一个危险的信号——人们可能低估了现有生活中潜在微塑料的占比。MPs可以在摄入，吸收和皮肤接触三种途径进入体内，以摄入为主要暴露途径。肠道是在摄入途径中MPs毒性作用的主要靶器官，因此研究肠道屏障损伤和MPs之间的动态关系是一个极好的切入点。在一定浓度下，微塑料（MPs）可能会损伤肠道屏障。已有文献证明，MPs的存在可能意味着肠道微生物多样性的降低。[1] MPs被证明可以显着减少弹尾肠的细菌多样性。在摄入污染物的动物肠道中被报道，有益菌（乳酸杆菌和链球菌）的数量减少。MPs对肠道的发育也带来负面影响，有报道发现摄入MPs后肠道壁因发育不良变薄，影响肠道的消化吸收。另外，MPs对环境微生物中的致病菌、微生物毒素和重金属具有一定的吸附作用，在多种实验中证明MPs及其吸附的有害物质会在肠道中积累并相互作用，破坏肠道的生物和免疫屏障，提供益于有害微生物菌株生长的肠道环境导致肠道内菌群失衡。肠道屏障的损伤暗示着一个不好的消息，肠道将会允许环境污染物进入体内循环，可能在其他器官里积累并引起全身炎症和代谢功能障碍。
这个部分需要稍微扩展一下，给几个数据，加个图片

结论

肠道是环境污染物毒性表征的主要部位。污染物在肠道的积聚造成了一些肠道屏障的问题进而可能会影响身体健康。在本文的整理中，人们对于环境污染物的低估可能意味着潜在的健康风险。一些活性物质和肠道菌群的探索可能是未来减少体内肠道积累的环境污染物的好主意。

keywords:
gut; environmental contaminants; remediation

Environmental Pollutants and Intestinal Health

author：Polaris

Background

Many experts have conducted diverse studies on environmental contaminants in the past. Traditional pollutants included polychlorinated biphenyls (PCBs), pesticides, heavy metals, and industrial pollutants (Wu et al.; Safe; Martin, Griswold and citizens); however, with greater industrialization and resource extraction, new pollutants primarily consist of perfluoroalkyl substances, microplastics, persistent organic pollutants, dioxin-like compounds, nanomaterials, medicines, artificial sweeteners, etc. (T. Wang et al.; Richardson and Kimura).

The lack of legislative limits on most emerging pollutants may indicate a high risk of pathogenicity. In recent years, a rising number of studies have revealed that contaminants can be found not only in the air but also in the soil and the water (Sarma). Consequently, contaminants accumulate in the food chain and are transferred to the human body (Muir et al.; Dudka, Miller and B).

The intestine is the first line of defense against foreign chemicals. There is a significant relationship between the gut barrier and environmental pollutants. It has been suggested that environmental contaminants harm the intestinal barrier by creating oxidative stress and affecting the gut flora, etc., causing sickness (L. Zhang et al.; Shil et al.; Campbell). In addition, it has been demonstrated that intestinal bacteria may degrade pollutants in the body and that substances that maintain the health of the gut have a role in facilitating the excretion of pollutants from the body (Yuan et al.; Keulers et al.). To address the gut health produced by environmental pollutants, this study aggregates a representative sample of gut impacts based on existing literature and uses this as a jumping off point to examine approaches to minimize the effects of environmental pollutants at two levels.

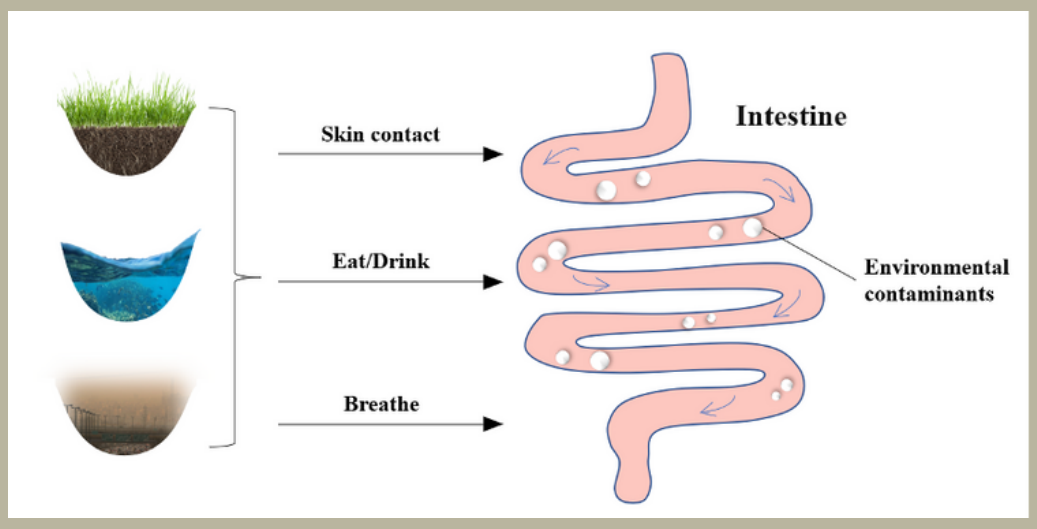


Figure 1: Migration of environmental pollutants.

Mitigating the effects of environmental pollutants on the intestinal tract

Even while they rid the body of potentially harmful pollutants, many drugs, including antibiotics, are connected to the development of adverse effects that patients would rather not experience. Making adjustments to one's food in order to maintain healthy intestinal function is becoming an increasingly frequent practice. Probiotics, prebiotics, and other functional foods with intestinal stability and various functional activities are some of the most well-established items that are currently available on the market for the regulation of dysbiosis of intestinal homeostasis. It has been established that seaweed polysaccharides, which are considered to be prebiotics, are good in preventing dysbiosis of the flora that is found in the gut (Ou et al.). There is evidence to suggest that a mixture of several distinct types of prebiotics can stimulate the growth of thick-walled bacteria while at the same time suppressing the growth of bacteria that are potentially pathogenic (Enterobacteriaceae) (Grazul, Kanda and Gondek). Herbal extracts that have the effect of modulating tight junction proteins and increasing the abundance of beneficial bacteria can also achieve the purpose of regulating the balance of human microbiota (L. Jin et al.), as indicated by experiments that were conducted on both cells and animals. Researchers from all over the world have come to the same conclusion, which is that certain strains of bacteria that have been isolated from the gut flora of certain animals have the ability to degrade MPs. It has been shown that bacteria that are naturally found in the digestive tracts of earthworms have the ability to lessen the overall size of MPs (Lwanga et al.). The ability to breakdown microplastics was discovered in Enterobacteriaceae strains that were isolated from the digestive tracts of wax moths (Ren et al.). According to the reports that are currently available, we are able to determine that the majority of the components that achieve the effect of repairing the intestinal barrier are active substances and have some kind of antibacterial effect. This opens up new doors for research into the screening of substances that have the ability to effectively mitigate any damage to the intestinal barrier that may occur in the future.

Conclusion

The gut is an essential location for measuring the toxicity of environmental contaminants. The accumulation of contaminants in the digestive tract creates problems for the intestinal barrier and has the potential to adversely damage health. Underestimating the environmental contaminants that exist may indicate the presence of potential health risks. In the future, it could be a good idea to investigate certain active substances and intestinal flora in order to cut down on the amount of environmental toxins that have collected in the intestinal tract of the body.

Discussion

Environmental pollutants damage the intestinal barrier

Research into the impact of recently found environmental pollutants on the digestive tract has garnered a far greater amount of attention than research into the effects of heavy metals. For the purpose of this investigation, we zeroed in on one type of newly discovered pollutant that is widely regarded as being particularly representative: microplastics (MPs). According to a previous study, there are approximately 5.25 trillion weighting 268,940 tonnes, plastic particles floating on the surface of the world's oceans (Eriksen et al.). A domestic investigation discovered that plastic residues have accumulated to 550,800 tonnes in the soil (D. Zhang et al.). This may be a warning sign since it shows that individuals may be underestimating the amount of potential microplastics in their actual life. Microplastics (MPs) have been identified in a number of studies to be present in the air, food, and products used in the house(Q. Zhang et al.; Fadare et al.). There are three ways that MPs can enter the body: by ingestion, through absorption, and through dermal contact; however, ingestion is by far the most prevalent method of exposure. Because the gut is a primary target organ for the adverse effects of MPs in the ingestion pathway, research into the interaction between disruption to the gut barrier and MPs is an excellent starting point. At some dosages, microplastics, also known as MPs, have the potential to cause damage to the barrier that lines the intestinal tract. Research has shown that the presence of microplastic particles (MPs) may be an indicator of a decrease in the variety of microorganisms that are prevalent in the digestive system (Medriano, Bae and Safety). MPs were shown to significantly reduce the bacterial diversity of the springtail gut (Ju, Zhu and Qiao). The quantity of beneficial bacteria (Lactobacillus and Streptococcus) in the guts of animals that ingested pollutants was shown to be diminished (Montero et al.). In addition to this, there is evidence that MPs can have a negative impact on the growth of the gastrointestinal tract, it has been claimed that after ingesting MPs, the intestinal wall becomes thinner due to dysplasia, which hinders digestion and absorption(K. Wang et al.). The ability of MPs to adsorb pathogenic bacteria, microbial toxins, and heavy metals from ambient microorganisms is also well documented (Huang et al.). It has been demonstrated in a number of experiments that microplastics (MPs) and the harmful substances that they adsorb accumulate and interact in the gut, thereby disrupting the biological and immune barrier of the gut and providing an intestinal environment conducive to the growth of harmful microbial strains, which in turn leads to an imbalance in the intestinal flora (Y. Jin et al.; Huang et al.). If the intestinal barrier is broken, this is bad news because it means that environmental toxins will be able to enter the circulation of the body and potentially accumulate in other organs, leading to inflammation throughout the body and metabolic dysfunction.

DENV

SMART 时报 vol. 1

I. Preface

(I) Introduction

Dengue fever, also known as dengue fever and dengue fever, is a tropical disease that is mainly transmitted by the mosquitoes Aedes albopictus and Aedes aegypti. The incubation period of dengue fever is 3 to 14 days. Symptoms include fever, headache, muscle and joint pain, and skin rash.

(II) History

The earliest recorded outbreak of dengue fever was in 1779. After World War II, dengue fever became a global public health issue, with at least 500 million to 528 million people infected each year and about 20,000 deaths, with an average mortality rate of 1% to 5%.

There was an outbreak of dengue fever in Taipei during World War II, and dengue fever has been absent in Taipei for decades since then. When the first case reappeared in the Taipei basin, the first reaction of experts from the Department of Health was disbelief. This case had never been abroad before and had never been to the central and southern parts of the country, and no spotted mosquitoes could be found at home, so where did the virus come from? The second and third cases occurred one after another, and what puzzled the experts was that they could not see any clusters, one time the cases appeared in Wanhua, Taipei, then suddenly in Beitou, then in Yonghe, then back to Zhonghe. At that time, a director of the Department of Health told reporters that "mosquitoes might have taken the train to Taipei", and this shocking statement made the front page. (This information is from "Key Battles - The Story of Infectious Diseases in Taiwan")

In the 20th century, people became more aware of the disease, and in addition to developing anti-mosquito programs, experts also worked on developing vaccines and drugs.

II. Main text

(A) Dengue fever virus (DEVN)

Virus classification: the virus belongs to the ribovirus domain and the mycovirus community flavivirus phylum Flaviviridae Flaviviridae dengue virus subgenus

DENV

Dengue fever virus is an RNA virus with an RNA length of about 11 kb, which can translate seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5) and three structural proteins (core, E, prM), and is divided into four serotypes (DEN-1, DEN-2, DEN-3, DEN-4) according to the difference of serum antigens. The molecular structure of these four viruses is similar, with a spherical shape and a diameter of 30 to 55 nm, and an icosahedral nucleus. Dengue fever virus enters the body and infects mainly dendritic cells. The virus binds to the DC-SIGN acceptor via ICAM-3 on dendritic cells, and the infected dendritic cells move to nearby lymph nodes to present antigens to T cells, initiating an immune response.

(ii) Vaccine
The earliest research on the dengue vaccine can be traced back to the 1950s, when scientists used laboratory rats to breed a less virulent Hawaiian strain of dengue virus and inoculated the subjects with it, thus saving them from dengue virus infection. From 1970 onwards, technology slowly advanced and scientists had different techniques to study the vaccine, thus dengue vaccine was developed.

Although this vaccine has entered clinical trials, researchers have found that the virus strain may transform into a highly pathogenic virus, which may cause fetal malformations in pregnant women.

DEN4Δ30: Deletion of 30 nucleotides in the untranscribed region of the DENV-4 gene, leading to the development of the first vaccine proven to be effective
TetraVax-DV: A mixture of four serotypes of dengue virus attenuated, but DENV-2 and 3 cannot be used in this way to achieve the same effect as DENV-1 and 4.

2. Active attenuated combination vaccine: Using other viruses of the yellow fever genus such as the Japanese encephalitis virus and dengue fever virus, the new virus has a low cure rate but can also make the human body immune.
CYD-TDV: Using YFV-17D as the backbone, together with the E and prM genes of DENV, clinical experiments have shown that the genotype is stable and the toxicity is low, and the protective effects against DENV1,2,3,4 are 61.2%, 3.5%, 81.9%, and 90% respectively.

DENVax: The E and prM genes of DENV1,3,4 were added to DENV-2, and the second phase of clinical trials has been completed in Thailand, Singapore, and the United States.

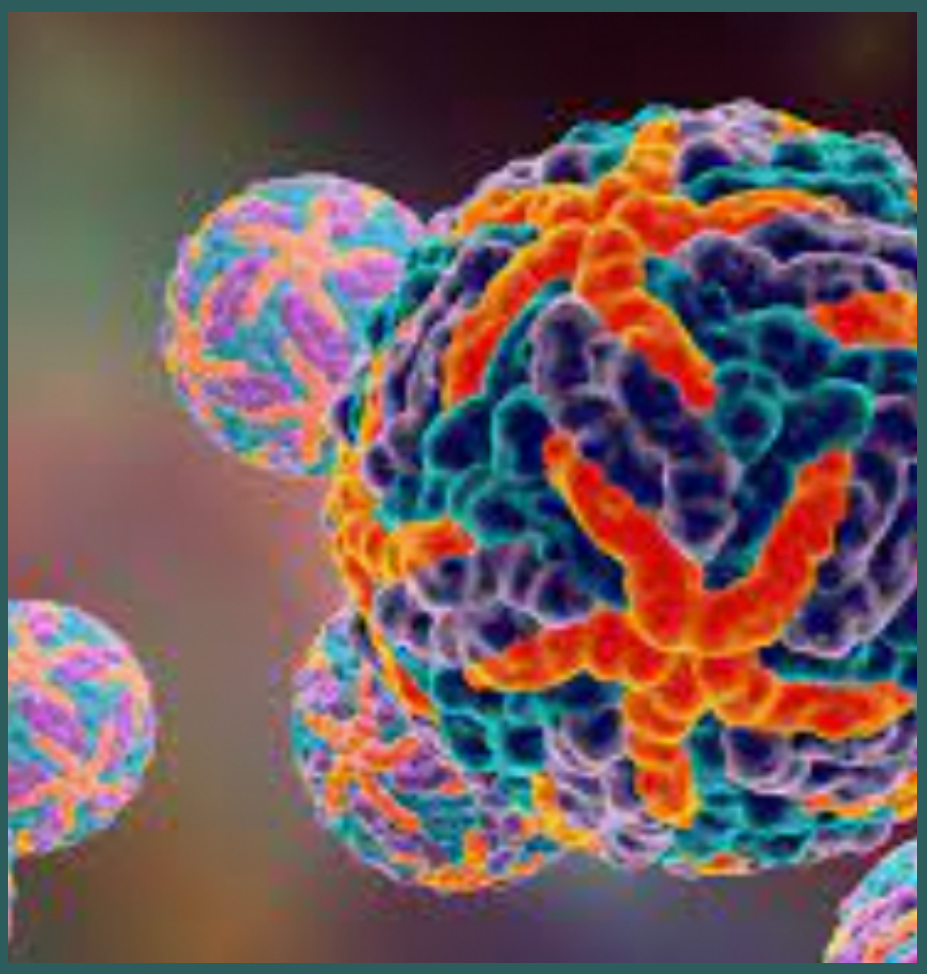
ChinDENV: developed by Chinese scientists, using the Japanese encephalitis virus vaccine as the backbone, embedded in the E gene of DENV-2, clinical trials have shown that it can resist not only DENV but also JEV

3. Inactivated vaccine: Dengue fever virus is deactivated by formalin, and then the antigen is extracted from the virus, and the antigen is used to induce immunity.
TDEN-PIV: Developed by GlaxoSmithKline (GSK), deactivated, and added with AS03B or AS01E adjuvant, clinical trials are underway in many regions.

III. Conclusion

(1) How to prevent and control?
Dengue fever is spread by mosquitoes of the genus Anopheles, which are characterized by white markings on their bodies. Do a good job of cleaning the environment, understanding dengue fever, and early medical attention for suspected symptoms, and reminding neighbors to avoid mosquito bites. To prevent mosquito bites, you can install screen windows and hang mosquito nets at home, and clean containers that may accumulate water to remove eggs by brushing. Patients infected with dengue fever should be prohibited from donating whole blood until four weeks after recovery, and family members, colleagues, and other contacts should hold off on blood donation for four weeks to prevent others from being infected by blood transfusion.

(II) Conclusion, Discussion
However, the global outbreak of dengue fever is due to the effects of global warming and the global greenhouse effect, which has caused dengue fever to spread worldwide in a short period of time from a few tropical countries. Otherwise, the virus crisis that human beings are facing will become more and more terrible.



IV. Citation information

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SMART Magazine

MRI's Application in Clinical Fields

1. Overview of MRI

1.1 Biomedical Imaging Modalities

MRI, the abbreviation of magnetic resonance imaging is a type of biomedical imaging modalities, which includes ultrasounds, medical radiation, computed tomography (CT), and nuclear medicine (planar scintigraphy, SPECT, PET). It is a medical imaging technique of using energy sources like light, lasers, X-rays, etc. Medical image modalities are often used in biology and medical fields. The images produced span orders of magnitude. As for MRI, it uses magnetic resonance, transmitting radio frequency energy and receiving radio frequency energy to produce images. The items that can be presented in the image produced by MRI include organs, muscles, bones, and blood vessels. One thing worth noticing is that MRI does not use any radiation and is completely non-invasive, which is also a reason why it's popular today.

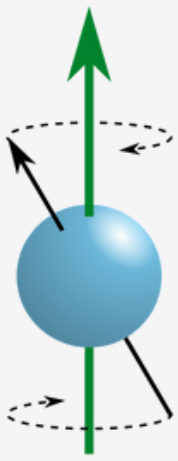
2. MRI's principles

The first step of conducting an MRI scan is to place a human into the magnetic field, which is usually in the form of an MRI machine. It is a cylindrical, tube-shaped machine that sends pulses of radio waves to create a strong magnetic field. The magnetic fields cause protons in the human body to align in the same direction, which is resonance, the R in MRI. The two aspects of the magnetic moment can be observed when protons are placed in a strong external magnetic field.

They either:

1. Align parallel or 2. Align anti-parallel to the external magnetic field.

When protons are in a steady magnetic field, they are randomly spread.

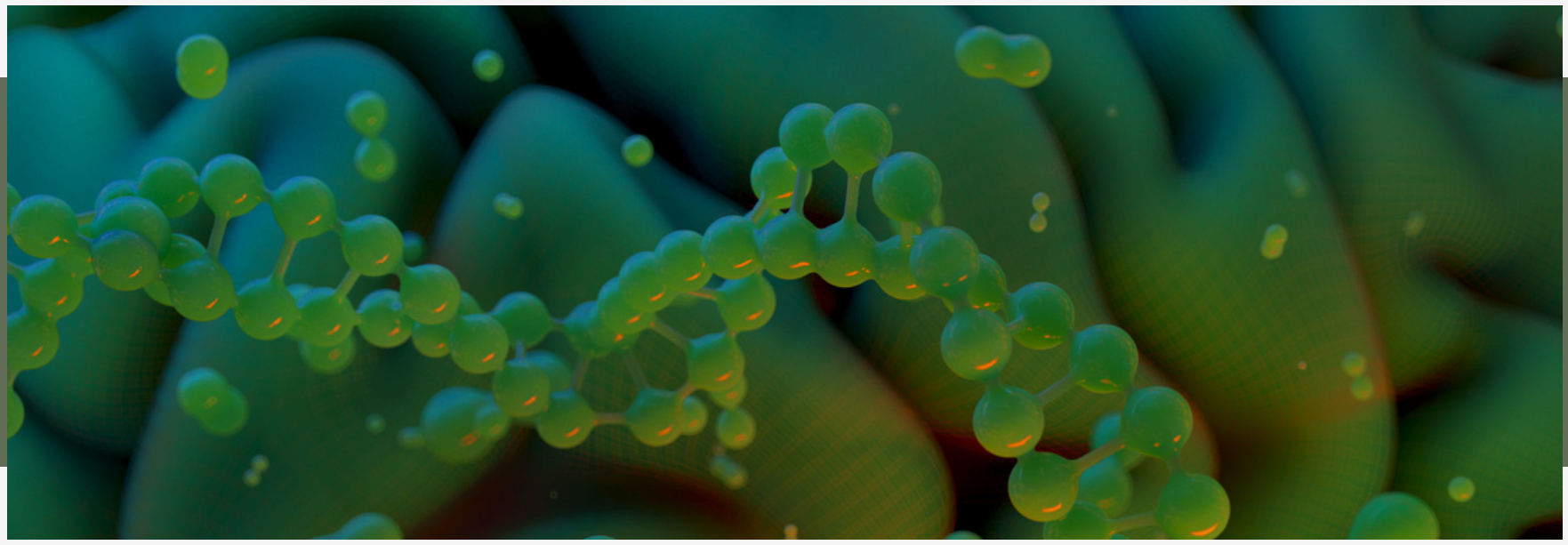


And then detect the radio waves sent from MRI machines. These signals will be collected into the computer and converted into an image. The protons which go parallel to the field have relatively lower states, and the anti-parallel to the field has a higher energy state. Most of them cancel each other, and the excessive amount is called spin excess.

Another phenomenon is precession. The processional path is around the magnetic field like gyroscopes. It is a vertically orientated gyroscope.

3. Current situation of MRI in clinical fields

Magnetic resonance imaging (MRI) is used today to look at organs tissues, skeletal systems, and structures inside the human body. After scanning, it will produce images of the body inside which are used for diagnoses, especially in fields of the brain and spinal cord. Several disadvantages of MRI which need improvement are the safety problems for patients who have metallic implants. The magnetic field will retain effects on the metal devices implanted in the body. Moreover, for patients who have Claustrophobia, MRI is also suffering because it is an enclosed place. Recent advances in MRI mainly focus on clinical operations, which as faster exam times, safer environment, and better image quality.



4. Application

Neurosurgeons highly rely on iMRI (intraoperative magnetic resonance imaging) to obtain accurate images inside of the brain which helps them in fields of brain tumors, epilepsy, essential tremor, Glioma Neuropsychiatric disorders, Parkinson's disease, Pediatric brain tumors, Pituitary tumors, etc.

Brain Tumor

The use of MRI has been a critical tool in neurosurgeon's armamentarium during tumor surgery. Research has shown it's better to remove more tumor issues. Meanwhile, these brain tumors are extremely complex. Removing healthy tissue could cause deficits, which means people have to be accurate when doing brain tumor surgery. With innovative surgical technologies such as intraoperative MRI, people can identify and locate brain tumors more precisely and recognize their relation to their vital brain centers, such as but not limited to: control of speech, strength, vision, etc. Doctors use iMRI to assist in surgery to treat, there're many benefits of iMRI. These include neuronavigation, compensation for movement, precision, mapping eloquent areas, and awake craniotomies. One of the biggest advantages of iMRI is its ability to precisely help locate brain tumors. The images generated are used during the surgery and serve as a guidance system. This directly solves the safety issues since it helps to identify and provide the safest surgical route to remove the tumor. During surgery, the organs on the side of the brain may shift, which will affect the precision of pre-surgical imaging. So the importance of having real-time iMRI images can be seen since people can adjust if needed according to the image produced by iMRI, which provides the actual position of the tumor. Another strength of iMRI is targeting the tumor embedded deep in the brain. MRI can be used in conjunction with functional MRI and other fiber-tracking technologies to visualize eloquent fields.

Dystonia

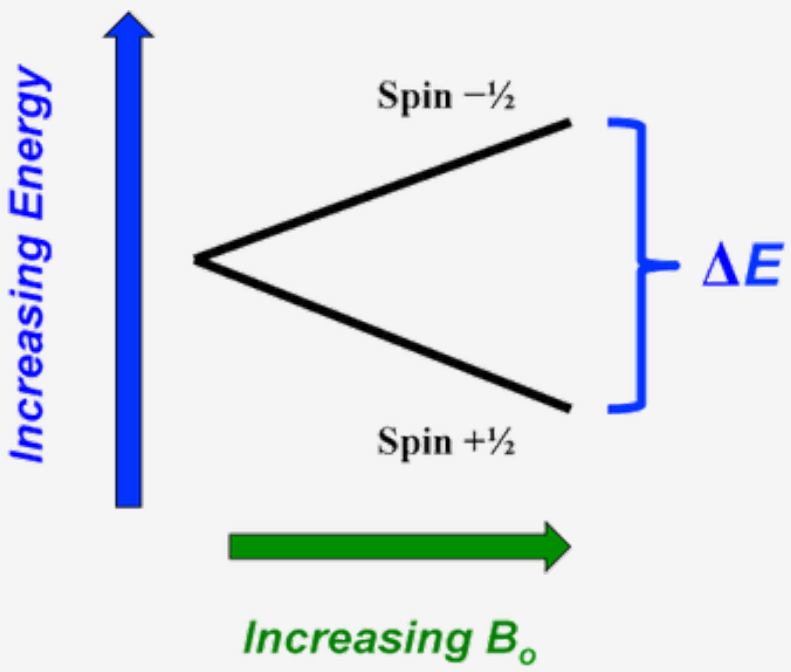
Dystonia according to Mayo Clinic is a movement disorder that causes muscles to contract involuntarily, including repetitive and twisting movement. It is a kind of neurological disorder linked to alterations in brain organization and environmental stressors and gene mutations. Neuro-imaging techniques had a substantial impact on the understanding of dystonia development, helping objective diagnosis and therapeutic interventions. It provides deeper insights into brain regional alterations at both structural and functional levels. Some recent improvements in apply of neuro-imaging in dystonia mainly focus on the attempt to link and understand the impact of gene mutations. Beginning with the discovery of DYT1. MRI help connects genetic factors and neural aberrancies.

Epilepsy

Epilepsy is a neuro disorder that happens in the central nervous system in which brain activity becomes abnormal and causes seizures. With symptoms like temporary confusion, stiff muscles, jerking movements of arms and legs, consciousness and awareness loss, fear, anxiety, déjà vu... MRI help to identify seizure and determine the proper seizure type. Tumors, malformations of cortical development, vascular malformations, mesial temporal sclerosis, and neocortical gliosis due to brain injury in epilepsy can be found on an MRI.

5. Notification before taking an MRI procedure

Because MRI is highly related to the magnetic field, any metal-made matters would affect the image. So patients need to report and remove any metal in the body. Consequently, it is required to remove all the piercings and leave all jewelry. If you are reporting it, make sure to include detailed information like the type of metal and location of metal, in order to determine the eligibility for MRI. As for food, drinks, and medications, people are allowed to have them as usual. Some people may need anti-anxiety medication due to claustrophobia. They may bring their prescription on the day of the appointment.



SMART Magazine

MRI在临床领域的应用

6. MRI advantages and disadvantages

As mentioned, no exposure to radiation and non-invasive is a huge advantage of MRI. It is also useful in scanning and detecting abnormalities in soft tissue. Thus, less likely to lead to an allergic reaction which may be caused by x-rays and CT scans.

The disadvantage of MRI scans focuses on their cost, health hazard, and the risk of creating negative feelings for patients. Since an MRI scan is conducted in an enclosed space with loud knocking noises made by magnets, it will make some people fear doing an MRI scan. In severe cases, it will harm hearing if adequate ear protection is absent. Some people might also feel a twitching sensation because it may cause peripheral muscle stimulation.

7. conclusion

Magnetic Resonance Imaging still has much room for improvement and innovation and is highly used for detecting and identifying disease while creating a safe surgery path for neurosurgery.

1. MRI的概述

1.1 生物医药成像模式

MRI是磁共振图谱的简称，这是生物医药成像的一种方式，它包括超声波、医学放射、计算机断层扫描，以及核医学（平面闪烁成像、单光子发生计算机断层成像术SPECT、正电子发射断层成像术PET）。这是一种使用例如光、激光、X-射线等能源的医学成像技术，通常被应用在生物学和医学领域。这种影像会产生巨大跨度，例如MRI，它利用磁共振传送射频能量并接受射频能量并成像。许多项目，例如器官、肌肉、骨骼、血管都可以呈现在MRI产生的影像中。一件值得注意的事是MRI并不使用放射性物质，它完全是非侵入性的，这也就是它到如今都受欢迎的原因。

2. MRI的原理

进行MRI扫描的第一步是将人放置在磁场中，它通常以MRI机器的方式存在。这是一个圆筒状的、管状的机器，可以发送无线电波脉冲，从而创造一个强大的磁场。这种磁场会造成人体的质子排列在同一方向，这就是共振，MRI中的R。当质子被放置在强大的外部磁场时，即可观察到磁矩的两个方面。

他们是：

1. 平行排列。
2. 与外部磁场反向平行排列。

当质子处在稳定磁场时，它们会进行随机的扩散。

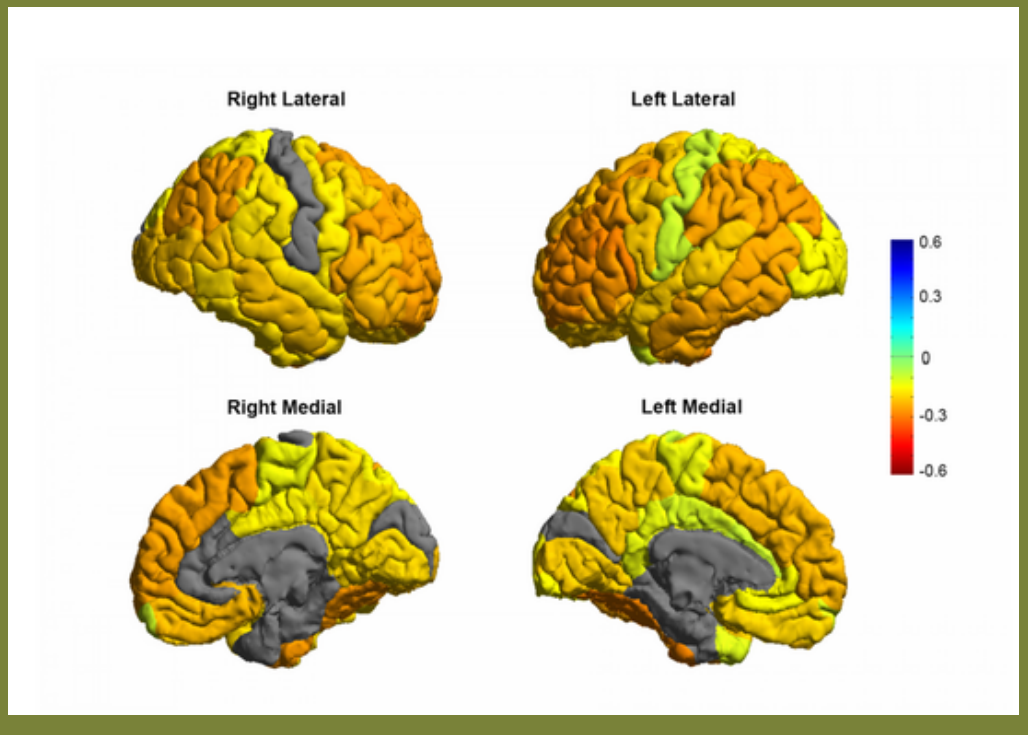
并且随后检测出无线电波由MRI机器发射。这些信号将会收集在电脑中并转变为图像。与磁场相平行的质子状态将对较低，而与磁场反向平行的质子有较高的能量状态。它们中绝大部分是相互抵消的，多余的总量被称为自旋余量。

另一种现象是运动。运动路径环绕磁场，像陀螺仪一样，这是一种垂直定向的陀螺仪。

3. MRI在临床领域的近期趋势

磁共振成像（MRI）如今被用来观察器官组织、骨骼系统以及人体内部的结构构造。在扫描过后，它将会生成人体内部用来诊断的成像，尤其是大脑和骨髓领域。MRI的个别需要改进的缺点有两点：含有金属移植物的病人的安全问题，磁场会持续影响人体内部被移植的金属设备；此外，具有幽闭恐惧症的病人也无法使用MRI，因为MRI设备是一个密闭空间。近期MRI的进展主要聚焦在临床操作，具有更快的检测时间、更安全的环境以及更好的成像质量。

神经外科医生高度依赖于iMRI（手术磁共振成像）获得精准的大脑内部成像。iMRI在脑瘤、癫痫、胶质瘤神经精神科紊乱帕金森疾病、儿科脑瘤以及脑垂体瘤等。



4. 应用

MRI的使用已成为肿瘤手术中神经外科医生设备的决定性工具。研究表明最好切除更多的肿瘤。同时，这些脑瘤却极其复杂，切除健康肿瘤可能会造成亏损，这意味着当进行脑瘤手术时，医生必须非常精准。使用新发明的外科技术例如iMRI，人们可以识别并更精准的定位脑瘤并识别出它们与至关重要的脑中枢的关系，包括但不限于：语言、力量、视觉的控制等。医生使用iMRI在手术中进行治疗，iMRI具有许多益处，包括神经导航、运动补给、精准性、绘制有说服力的区域以及进行开颅术。iMRI最大的优点之一是它的精准定位脑瘤的能力，生成的图像在手术期间使用并作为指导系统服务。当它帮助识别并提供切除肿瘤的最安全的手术路线时，就可以直接解决了安全性问题。在手术期间，大脑中的器官可能会移动，这将会影像术前图像的精准性。所以当人们根据iMRI生成的图像进行调整时，拥有实时iMRI成像的重要性也显现了出来，及它可以提供肿瘤的实际位置。iMRI的另一个优势是针对嵌入大脑深处的肿瘤，MRI可以与功能性MRI和其他的光线追踪技术共同使用，形象化有说服力的区域。

肌张力障碍

梅约诊所提出的肌张力障碍是一种造成肌肉不自主收缩的运动紊乱，包括重复和扭曲的运动。这是一种与大脑组织的改变、环境紧张性刺激和基因突变有关的神经性紊乱。在结构和功能水平上大脑局部改变中它提供了更加深刻的见解。在肌张力障碍神经成像的应用方面，最近的改善主要聚焦于试图联系并理解基因突变的影响。开始发现DYTI时，MRI有助于连接遗传因素和神经异常。

癫痫

癫痫是发生在中枢神经系统的神经紊乱，在中枢神经系统中大脑行为变得不正常、造成痉挛并伴随一些症状，例如暂时性混乱、肌肉僵硬、四肢运动颠簸、知觉意识丧失、恐惧、焦虑...某日有助于识别癫痫并确定正确的癫痫种类。一些由于癫痫时大脑的损伤，例如肿瘤、皮质发育畸形、管脉畸形、内侧颞叶硬化、皮质神经胶质过多症等都可以被MRI查出。

6. MRI的优点和缺陷

正如之前所提及，无放射暴露以及非侵入式是MRI的一个巨大的优点。它同时也有助于扫描并检测软组织异常。因此，它不太可能导致由X射线和CT扫描引起的过敏反应。

MRI的缺点主要集中在它们的价格、健康风险以及对病人产生负面情绪的风险。由于MRI是在伴随由电磁产生的巨大敲击声的密闭空间中进行的,这将会是的一些人害怕做MRI扫描。在严重情况下，如果缺乏对耳朵的保护，这将会造成听力损伤。一些人可能也会感觉到抽搐，因为，MRI可能会造成外源肌肉刺激。

5. 进行MRI检查前注意事项

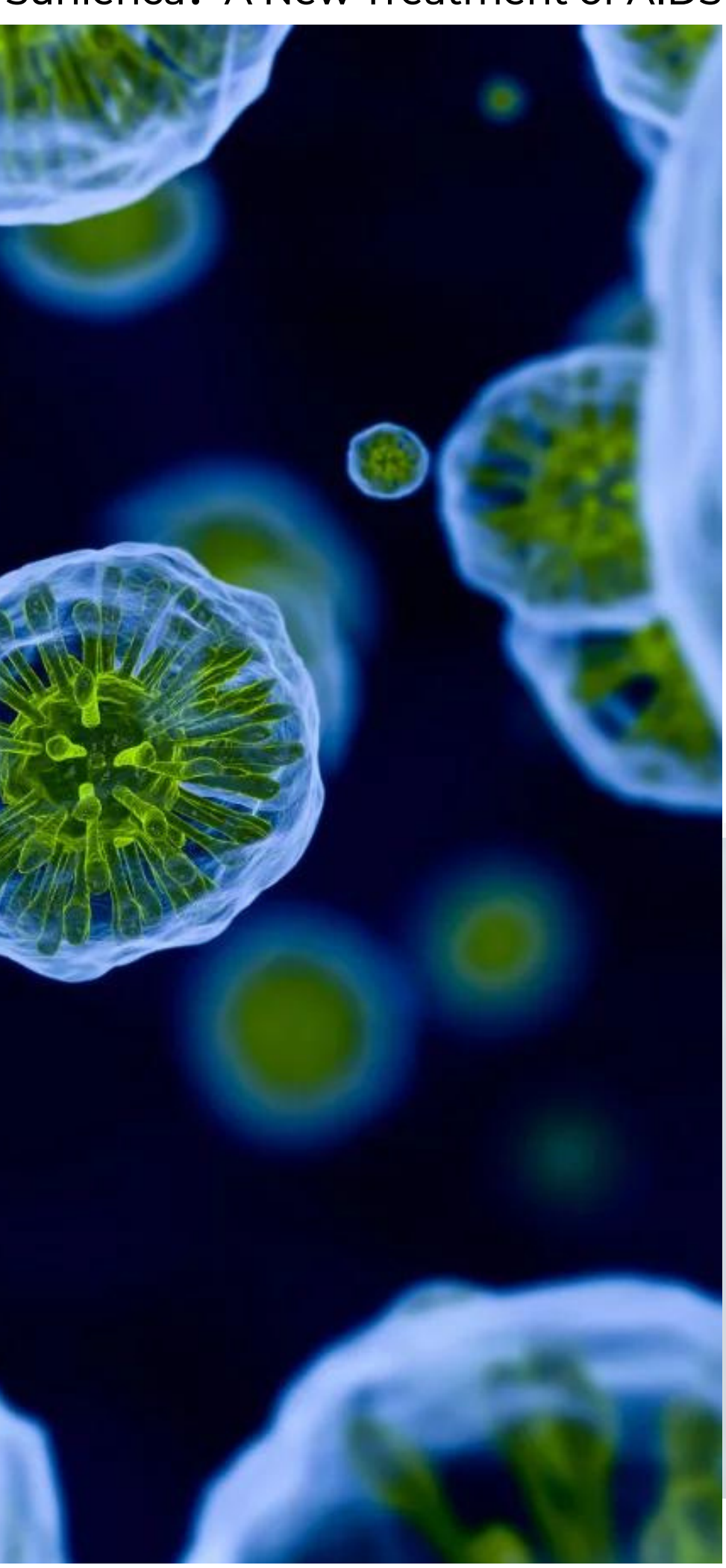
由于MRI与磁场高度相关，任何金属制品都会影响图像，所以病人需要汇报并移除身体内的任何金属。及它需要移除所有的穿刺和珠宝。如果你想汇报他，请确保包含的详细信息，如金属类型和金属位置，以确保MRI的使用。对于食物、饮料、药物，人们可以像往常使用。一些人由于幽闭恐惧症可能需要抗焦虑药物，他们可以在约定当天带着他们的药方。

7. 结论

磁共振成像仍然有很大的改进和创新空间，在为神经外科创造安全手术途径时，MRI被高度用于疾病的检测和识别。

SMART Magazine

Sunlenca：A New Treatment of AIDS



Getting To Know About AIDS

Initially started since the last centry, an unknown desease spread across the world. The desease then was named as AIDS, by it's full name of acquired immunodeficiency syndrome. It literally means a disease caused by being infected with HIV, human immunodeficiency virus. HIV is single-stranded RNA virus, is a group of Retroviridae - Lentivirus - Human Lentivirus.It can be devided as HIV-1 and HIV-2 according to genetic difference.HIV-1 is the main prevalence virus strain. The major propagation methods are Sexual Transmission, Mother-to-Child Transmission, and Blood Transmission. Clinically, it is mainly divided into four stages, including acute infection period, incubation period, symptom period and onset period. Most infected patients will not experience obvious symptoms at the initial stage of infection, and some infected patients may occur symptoms similar to influenza.

Ever since the discovery of HIV，more than 70 million people have infected it globally. Although the total number of infected patients continues to increase, but with effective treatment and prevention measures, the public has begun to understand the virus of AIDS.And the number has slowed down in recent decades, and the amount of fatality is declining.

Methods of Treating AIDS

The treatment of AIDS started with monotherapy, for example, zidovudine is the first anti AIDS drug, but this treatment is prone to drug resistance. Today, cocktail therapy, also known as HAART, Highly Active Antiretrovirus Therapy, has become the most effective treatment. It uses three or more antiviral drugs and reduced drug resistance.

What is Sunlenca?

Although there are antiviral drugs that can effectively inhibit AIDS virus effectively, some patients still shows cross resistance. And Sunlenca (Lenacapavir),a capsid inhibitor, plays an important role when it comes to this situation. Sunlenca is a new type of antiretroviral drug. The forms of medication consists oral tablets and subcutaneous injection. It is used in combination with other antiretroviral drugs to treat adult patients infected with HIV-1. patients choose their own treatment plan according to their own needs, making the combination change more flexible and reducing the problem of drug resistance.

The drug takes effect by blocking the protein coat of the virus, thereby destroying the life cycle of the virus.Sunlenca has no cross-resistance with existing drugs, so it is a breakthrough in treating patients with multiple drug resistance. In addition, patients with multiple drug resistance Sunlenca only needs to conduct subcutaneous injection of Sunlenca once every six months , which greatly improves the compliableness of the patients, reduces the nursing burden, saves a lot of time for patients, and achieves the goal of long-term treatment at the same time. On August 22, 2022, the European Commission (EC) granted the marketing license of Sunlenca (Lenacaavir) developed by Gilead Sciences, and on December 22, the United States Food and Drug Administration (FDA) also approved the marketing application of Sunlenca. However, now only the United States, Canada and EU member countries have approved the use.

Clinical Trial of CAPELLA

The clinical trial of CAPELLA is a 2/3 phase, double-blinded, placebo-controlled global multi-center study to evaluate and improve the treatment scheme and safety of Lenacaavair. The conclusion is that at the 52nd week, 83% of patients who received Sunlenca combined with other drugs could not detect the viral load. In terms of safety, Sunlenca's adverse reactions during treatment are also very mild, and nausea and swelling at the injection site are only few.

Based on the long-term effectiveness and safety of Sunlenca, it is one of the effective programs to suppress AIDS virus. In the future, it is hoped that drugs can reduce the price and improve the popularity of drugs. I think it is still uncertain whether this investigational drug will be commercialized in the future. Although the effectiveness and safety of this drug are relatively good according to CAPELLA's data, I personally think there are still many uncertain factors in it, which can be determined only after repeated human experiments.

Sunlenca一种新的艾滋病治疗方法

了解艾滋病

由上个世纪开始，一种不明疾病席卷全球，而该病毒称为艾滋病(AIDS：acquired immunodeficiency syndrome)，全名为获得性免疫缺陷综合症，字面意思就是由于人类免疫缺陷病毒(HIV:human immunodeficiency virus)感染所造成的疾病。艾滋病属于单链RNA病毒，为逆转录病毒科-慢病毒属-人类慢病毒组。根据基因的差异分为HIV-1型和HIV-2型，而HIV-1为全球主要流行病毒株。艾滋病主要通过性、血、母婴三种途径传播，临床上主要分为四个阶段，分为急性感染期、潜伏期、症状期以及发病期，大部分感染者在感染初期并不会出现明显病症，部分感染者可能有类似流感的病症。

自艾滋病病毒发现以来，全球超过七千万人感染，虽然艾滋病感染人口总量还在不断增加，但是由于有效的救治以及预防对策，大众对于艾滋病这个病毒开始有所认识，近几十年来有放缓的迹象，同时死亡人数正在下降。

治疗艾滋病的方法

艾滋病的治疗最开始为单药治疗，例如齐多夫定（zidovudine)就是第一款抗艾滋病的药物，但是该治疗方案很容易产生耐药性。时至今日，鸡尾酒疗法(cocktail therapy)，又称为高效抗逆转录病毒治疗(HAART:Highly Active Anti-Retrovirus Therapy)成为最有效的疗法，该疗法使用三种或以上的抗病毒药物进行治疗，降低耐药性。

Sunlenca是什么?

虽然现今已经有抗病毒药物可以有效抑制艾滋病病毒，但是某部分的患者体内仍有交叉耐药性的表现，Sunlenca(Lenacapavir)作为一种衣壳抑制剂就在这个时候发挥重要作用。Sunlenca是一种新型抗逆转录病毒药物，起始剂量为口服片剂和皮下注射，与其他抗逆转录病毒药物联合使用，用于治疗患有HIV-1型的成年患者。患者根据自身的需求，选择适合自己的治疗方案，使得组合变化更为灵活，降低耐药性的问题。该药物通过阻断病毒的蛋白质外壳起作用，从而破坏病毒的生命周期。Sunlenca与现有药物不存在交叉耐药性，所以对于治疗多重耐药性的患者为一大突破。而且Sunlenca只需为多重耐药性的患者每六个月进行一次皮下注射，大大地提高了患者的依从性，减轻护理负担，节省了患者大量的时间，同时达到长效治疗的目的。就在2022年8 月22日，欧盟委员会(EC)授予吉利德(Gilead Sciences)所研发的Sunlenca（Lenacapavir) 上市许可，而在同年的12月22日，美国食品药物监督管理局(FDA)也批准Sunlenca的上市申请。但是现阶段只有美国、加拿大以及欧盟成员国批准使用。

CAPELLA临床实验

有关CAPELLA的临床实验，是一项2/3期、双盲、安慰剂的对照全球多中心研究，在于评估Lenacapavir的优化治疗方案以及安全性。而结论得出，在第52周时83%接受Sunlenca与其他药物合并治疗的患者基本上检测不到病毒载量。而且就安全性方面，Sunlenca在治疗的过程中所出现的不良反应也十分轻微，恶心以及注射部位肿胀只是占少数。

基于Sunlenca的长效性以及安全性，是其中一种抑制艾滋病病毒的有效方案，未来希望药物可以降低价格，提高药物的普及性。对于将来这种研究性的药物会不会商业化，我觉得现在暂时还未确定，虽然由CAPELLA的数据得出，该药物的有效性以及安全性较为良好，但是我个人觉得还有很多不确定因素在当中，要反复进行多次的人体实验才可以确定。

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